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RECENT ADVANCES IN LIVER DISEASE

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I. CIRRHOSIS

Cirrhosis implies fibrosis involving all parts of the liver, accompanied by nodular parenchymal regeneration. Necrosis of hepatic cells occurs at some stage.[1]

A. TYPES OF CIRRHOSIS

1. Portal and Post-necrotic Cirrhosis

These are the two common types of cirrhosis. Both terms are unsatisfactory, and intermediate forms occur. The name 'portal' is used when every lobule of the liver is involved, the connective tissue is in thick regular bands, and there are small regenerating nodules throughout the liver. This type is commonly associated with alcoholism. Post-necrotic cirhosis denotes the presence of bands of fibrous tissue of varying thickness, nodules varying in size, and normal lobules within the larger nodules. The name Laennec's cirrhosis should be used to denote the terminal picture of either portal or post-necrotic cirrhosis.[2]

Aetiology

The role of viral hepatitis in the aetiology of cirrhosis remains controversial. Zieve *et al.*[3] examined 367 men who had had acute viral hepatitis 4 - 6 years earlier and showed that there was no greater incidence of liver disease amongst them than amongst normal controls. Cullinan *et al.*[4] followed up 91·6% of 1,293 cases of infectious hepatitis which occurred amongst British servicemen in the Middle East in World War II, and failed to find a single case of cirrhosis. Despite these reports, many accept the concept of post-hepatitic cirrhosis in civilian practice. This is based on a previous history of infective hepatitis in patients who have post-necrotic cirrhosis. Howard and Watson[5] obtained such a history in 17% of their patients. Sherlock[6] obtained it in 33% of her series of cirrhosis cases, and 50% of her patients had no detectable cause for their disease.

MacKay and his co-workers[7,8] discussed auto-immunization as the cause of some cases of cirrhosis. It seems possible that some substances in the liver cells might become antigenic, either because structural changes make them more accessible to the blood or as a result of damage by virus infection or malnutrition. It has been demonstrated that serum from patients with acute hepatitis may fix complement in the presence of human liver homogenate and this is presumed to be due to the presence of antibody-like substances in the serum. This reaction tends to become negative as the patient recovers from hepatitis. Most cases of chronic active hepatitis have a low titre when tested, and the highest titres have been obtained in 'lupoid hepatitis'.[8] Further research is in progress along these lines.

The nature of the association of alcoholism with portal cirrhosis is not clear, but it is estimated that 8% of alcoholics develop this complication.[9] Alcohol may cause an increase in the serum levels of glutamic oxalacetic transaminase and of glutamic pyruvic transaminase, indicating that liver damage, probably liver-cell necrosis, is sometimes caused by alcohol itself.[10] Only 18% of cirrhotics in England are alcoholics, but in New York the comparable figure is 54%, and it seems that in these patients malnutrition may be an important factor in the genesis of their cirrhosis. The relatively high intake of carbohydrate on the part of these patients has been incriminated in the past. It is well known that alcoholics suffer from protein malnutrition and it is possible that long-continued malnutrition may itself result in cirrhosis or may render the liver more susceptible to noxious agents.[11] The cirrhosis which occurs in the African, and is a precursor of liver carcinoma, may have the same aetiology. It is of great interest that long-term follow-up on children who have suffered from kwashiorkor has failed to reveal any evidence of hepatic fibrosis.

The work of Himsworth[12] highlighted the results of experimental dietary depletion in animals. Choline deficiency regularly produces diffuse fatty change in the liver of the rat, and this is followed by a diffuse fibrosis, which in turn results in an atrophic nodular cirrhosis.[13] To what extent these experimental results can be applied to human disease is unknown.

2. Cirrhosis from Other Causes

(a) Hanot's Biliary Cirrhosis (Chronic Intrahepatic Obstructive Jaundice)

This usually affects women between the ages of 35 and 70 and is rarely seen in males. The aetiology is unknown. Characteristically, the onset is insidious, with pruritus often preceding the jaundice by months or years. The jaundice is obstructive and is of varying degree. The patient feels well, has no abdominal pain or fever, is pigmented, may show skin xanthoma, and has a large, firm, smooth liver with an enlarged spleen and steatorrhoea.

The presence of urobilin in the urine and stercobilin in the stool indicates that the obstructive jaundice is incomplete. The serum alkaline phosphatase is considerably raised, as are the cholesterol and total lipids and the $\alpha 2$ and β globulins. The prognosis is relatively good.

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(*b*) *Secondary Biliary Cirrhosis*

This occurs after long-standing obstruction of the extra- or intrahepatic bile-ducts; e.g. from calculus, traumatic stricture, congenital obliteration, or neoplasia.

(*c*) *Haemachromatosis*

In this disease there is an increase in total body iron, an increased serum-iron concentration and a raised saturation of the iron-binding capacity. It seems likely that haemachromatosis is due to an inborn error of metabolism resulting from an autosomal genetic defect of incomplete penetrance and/or variable expressivity which is transmitted as a Mendelian dominant.[14] About 20% of relatives of affected patients have elevated serum-iron levels and are therefore likely to develop the full picture of the disease in later life. It is probable that early treatment by repeated phlebotomies designed to bring the serum iron to normal levels, and keep it there, will prevent the development of the disease. The full syndrome is characterized by cirrhosis, diabetes, skin pigmentation, genital atrophy, loss of body hair, and cardiac involvement. Cardiac involvement occurs in 30% of cases and may lead to cardiac failure. Two further points should be made:

(i) There is still no proof that the deposition of iron directly causes the cirrhosis,

(ii) The rare occurrence in a young female is probably the occurrence of the disease in the homozygous form.

(*d*) *Hepatolenticular Degeneration* (*Kinnear-Wilson's Disease*)

This should be suspected if a patient with cirrhosis has signs of extrapyramidal disease, and an intention tremor in addition. A greyish-green corneal ring is present in 90% of cases. This rare disease often causes a low serum uric acid and a low serum phosphorus owing to urinary loss, and these are useful screening tests. The fundamental disturbance in copper metabolism is a deficiency in the synthesis of ceruloplasmin, the serum protein which normally binds and carries copper in the serum. The result of this is that the copper is loosely bound to serum albumin instead and is readily deposited in the liver, basal ganglia, and renal tubules. Treatment is with BAL or penicillamine, which is a copper-chelating agent. Some patients have improved on this treatment, but it must be continued for a long time. The response does not seem to be as good in severely affected young patients. There is a high incidence of consanguinity in the patients' parents. It is not yet certain that the increased liver copper itself is responsible for the cirrhosis.

(*e*) *Cardiac Cirrhosis*

This may occur incidently in cardiac failure of long duration.

(*f*) *Cirrhosis in Young Women*

In recent years reports from many parts of the world[15,16] have described a variety of cirrhosis with special features in young women. The patients are usually under the age of 35 years and the syndrome is rarely seen in males. They are mildly jaundiced and feel well but have periods of fever and polyarthritis. Acne is often present. Moon-shaped facies, abdominal striae and amenorrhoea are commonly noted. Ascites occurs terminally. The serum α globulin is high. Occasionally the Wassermann reaction is falsely positive and lupus erythematosus cells are found. For this reason the term 'lupoid hepatitis' has been used and some believe that the condition may be related to systemic lupus erythematosus.[7] It seems likely that it is not a variant of this systemic disease, but rather a non-specific reaction by the liver of the young woman. About half the patients have a previous history of acute hepatitis.[6] It is in the aetiology of this syndrome that the possible role of auto-immunization has received most attention in the field of liver disease. Cortisone treatment has its best results in patients who are more deeply jaundiced and have high serum α globulin; it sometimes results in clinical, biochemical and histological improvement. While it is not certain whether steroids should be used for long-term treatment, it seems wise to restrict their use to acute exacerbations of the hepatic process or other complications, e.g. polyarthritis, and to stop them as soon as possible. Even without treatment the prognosis is quite good.

B. MANAGEMENT OF PATIENTS WITH CIRRHOSIS

1. Cirrhosis without Complications

A good diet and total abstention from alcohol is important in the treatment of well-compensated cirrhosis. One should aim at about 2,500 calories a day with a protein content of 100 g. There is no evidence in favour of added choline or methionine, but vitamin supplements are usually given. If an associated anaemia is due to blood loss from varices, then it will respond to oral iron, but the anaemia of liver disease itself, which may have a latent haemolytic element, may not respond to iron, and blood transfusion is often necessary to maintain the haemoglobin at an adequate level. Sedatives should be avoided if possible. Pethidine should be preferred to morphine because of the liability of the latter to precipitate coma. Paraldehyde may precipitate coma too, and barbiturates should be used with great care. It is doubtful whether the course of the disease is changed by the use of cortisone or allied compounds.

2. Cirrhosis with Complications

(*a*) *Hepatic Pre-coma and Coma* (*Porto-systemic Encephalopathy*)

This is diagnosed when the patient develops all or some of the following symptoms and signs: Disturbed level of consciousness, particularly drowsiness by day and wakefulness at night; intellectual and personality changes; slurred speech; and a 'flapping' tremor of the hands best demonstrated when the arms are outstretched, the fingers separated, and the wrists hyperextended. The tremor may become more generalized and may result in ataxia; it is also seen in uraemia and respiratory failure associated with hypercapnia. Pyramidal signs may be elicited in the limbs, but plantar responses are often flexor. Foetor hepaticus is smelt in the breath and occurs not only in liver failure but also in any patient with extensive portal collateral circulation, e.g. after operative portocaval shunts, and is not in itself diagnostic when such collaterals are present. A high level of ammonium is often found in the blood and ammonium salts may precipitate coma. This led to the concept of the toxicity of ammonia and to the efforts to lower it in treatment.

Glutamic acid has been given because it combines with ammonia to form glutamine.[17] Arginine has been tried because it is said to 'stimulate' the Krebs cycle in the liver and so to encourage the detoxication of ammonia to urea.[18] It is true that both glutamic acid and arginine sometimes reduce blood-ammonia levels but neither is consistently successful in treatment.[19] It is unlikely that either will become

part of the routine treatment of hepatic coma. Artificial dialysis with the artificial kidney is probably only of use, if at all, in patients in whom the coma has been precipitated by a large gastro-intestinal bleed, and these patients have a better prognosis in any event.[6] Ion-exchange resins have also been used to lower the blood ammonia.[20] It seems likely that coma is due to a number of noxious agents[21] and that the elevated blood ammonia is only one of these. It is therefore not surprising that there is no good correlation between the blood-ammonia level and this syndrome. There is good evidence for the belief that some toxic substances may result from the breakdown of protein in the gut. These substances are then absorbed but not detoxified by the diseased liver, or are shunted past it by the collateral circulation, and so reach the systemic circulation and cause the syndrome.

This is the corner-stone of treatment—*protein restriction.* At the first sign of pre-coma the patient is given a protein-free diet; 20% glucose by the mouth usually provides adequate calories. Caval catheterization is avoided if possible, owing to the high incidence of infection associated with it. To prevent intestinal bacteria from breaking down protein, a broad-spectrum antibiotic is given by mouth, e.g. neomycin 1 g. 4-hourly for 1 week. It is of great importance to detect a *precipitating cause* and to treat it if possible; e.g. overdosage with morphine or barbiturates; the use of chlorothiazide, possibly through its hypokalaemic effect; haemorrhage from varices, operations, alcohol ingestion and infection; and the aspiration of ascites. Coma due to one of these precipitating factors carries a better prognosis. When there has been haemorrhage into the gastro-intestinal tract some authorities advocate washing the stomach free of blood to reduce the absorption of the products of digested blood.

Porto-systemic encephalopathy does not always present acutely, and in the more chronic cases treatment does not have to be so vigorous and a small amount of protein may be allowed in the diet. The limit of tolerance for each patient has to be determined. Patients treated with a high-protein diet who develop porto-systemic encephalopathy should be put on a protein-free diet until the signs of this complication have disappeared. Protein can then be reintroduced to the limit of tolerance. Broad-spectrum antibiotics are only used for acute exacerbations in these chronic patients, although in some it may be necessary to use them for long periods of time. Enemata and purges of magnesium sulphate are useful in keeping the bowel free from nitrogenous substances in the acute cases. There are conflicting reports on the use of cortisone and related compounds in the treatment of hepatic coma;[22,23] they are not usually of any value.

(*b*) *Ascites*

Abdominal paracentesis should be performed as *infrequently* as possible. This is because the ascitic fluid is rich in protein, and repeated aspirations result in considerable protein loss in a patient who is unable to synthesize protein adequately. The keynote of treatment is restriction of salt and rest in bed. A patient with ascites usually excretes 5 - 10 mEq. of sodium in the urine daily. The loss from other sources such as sweating is usually about 22 mEq. so that any intake in excess of about 30 mEq. will be retained probably as a result of secondary hyperaldosteronism. Dietary sodium must not exceed 22 mEq. a day and this can be achieved by cooking without salt, eating salt-free bread and butter, and avoiding foods with a high salt content, e.g. pastries cooked with baking soda. Protein-rich foods contain salt. These patients require a high-protein diet, and so some meat and fish is essential, and the use of salt-poor protein supplements make the diet rich in protein while remaining poor in salt. Mersalyl and the chlorothiazide group of drugs are of great value. The action of mersalyl can be potentiated by the use of potassium chloride rather than ammonium chloride and, when the chlorothiazide group is used, potassium supplements are usually necessary and should be given on the days on which chlorothiazide is not being given. Chlorothiazide has been shown to precipitate coma in some patients and a careful watch should be kept for this complication.[24] Aldosterone antagonists (spirolactones) have been used with variable success in resistant cases.[25] Intravenous salt-poor human albumen and ion-exchange resins have not proved of much value. If there is no response to a fair trial of treatment the prognosis is poor.

(*c*) *Portal Hypertension*

Apart from ascites the important complication of portal hypertension is haemorrhage from oesophageal or gastric varices. Patients with cirrhosis, particularly alcoholics, may be bleeding from a peptic ulcer or from gastritis and not from their varices, and the differential diagnosis is sometimes difficult.[26] In doubtful cases, oesophagoscopy and gastroscopy may have to be resorted to, but the presence of large amounts of blood may make interpretation difficult, and it has been advised that the stomach should be washed out with iced water before endoscopy. Biochemically, the blood ammonia is raised in 87% of cirrhotics after haemorrhage into the gastro-intestinal tract, and the retention of bromsulphalein is abnormal in 93%. Bromsulphalein is retained to above 15% in 25% of non-cirrhotics, and the blood ammonia is normal in 95% of non-cirrhotics after haemorrhage. On the basis of these findings it has been suggested that in upper gastro-intestinal bleeding a blood ammonia of above 150 μg% and a bromosulphalein retention of above 15% are diagnostic of cirrhosis when taken together, while if both are normal there is no cirrhosis.[27] This might be useful in excluding cirrhosis, but even when the presence of cirrhosis is confirmed, an ulcer and not the varices may be responsible for the bleeding. Control of the haemorrhage by the Sengstaken tube suggests that the source is variceal. Emergency barium meal and splenic venography may be useful in selected cases.

The treatment of massive haemorrhage from oesophageal or gastric varices is blood transfusion to replace the blood lost. Sedation should be confined to small doses of barbiturates. Sherlock[6] advises that patients with cirrhosis (as opposed to those with varices on the basis of extrahepatic portal block) should be treated for incipient hepatic coma with glucose and neomycin. In this way neurological complications may be prevented. If bleeding continues, a Sengstaken tube should be passed and an attempt made to control the bleeding in this way. The use of this tube requires great care, and those using it should be fully conversant with the possible complications.[6] Results are variable. The tube often stops the bleeding only for it to recur when it is removed; reinsertion is then necessary. It is an unsatisfactory form of treatment, but the best available at present.

Attempts to lower portal venous pressure in an effort to prevent further haemorrhage must be preceded by portal

venography, which will demonstrate the extent of the collateral circulation and the patency of the portal vein. The latter is essential if a porto-systemic anastomosis is to be performed, which is the operation of choice. It should not be undertaken before the initial haemorrhage,[28] and is performed in an attempt to prevent repeated haemorrhage. Whether it is sufficiently successful in this will be shown by longer periods of follow-up than are at present available.[29] Porto-systemic encephalopathy may follow these artificial-shunt operations. This becomes more likely if there is any evidence of encephalopathy beforehand. Latent pre-operative porto-systemic encephalopathy can be detected by various tests, e.g. forced protein feeding and serial electroencephalographs, and if any tendency towards the development of this complication is detected, the operation is contra-indicated. As a general rule, older patients and patients with inadequate hepatic functions are unsuitable for porto-systemic shunts. The serum bilirubin, also, must be less than 1·5 mg.% and the serum albumin more than 3 g.%. Ascites is usually a contra-indication, although selected cases with ascites and with good hepatic functions have been operated upon, but the results are variable. Hepatic wedge pressure[30] is helpful in distinguishing between intra- and extrahepatic causes of portal hypertension. In cirrhosis it is raised while in obstruction of the portal vein it is normal. In both, the splenic pressure is raised. Recently portal hypertension has been described in the absence of cirrhosis, portal-vein obstruction, or any other detectable cause. It has also recently been confirmed that posterior pituitary extract reduces portal venous pressure in dogs with end-to-side porto-systemic shunts. As the portal venous pressure falls, so the oxygen saturation falls too, and it is possible that posterior pituitary extract may act by closing arteriovenous shunts in the stomach and bowel. Extensive vascular shunts are known to exist in cirrhosis in man and, when they occur in the pulmonary circulation, they may cause systemic anoxia and central cyanosis.

In the treatment of massive uncontrollable haemorrhage from varices, one of a series of operative methods may be attempted, such as resection of the oesophagus or stomach, carried out as an emergency procedure. These operations have a very limited success and emergency portocaval anastomosis is preferable, but not usually possible during the bleeding episode. Ligation of the hepatic artery is not indicated.

II. HEPATITIS

Acute viral hepatitis is the commonest form of liver disease seen in practice. It is usually mild and in some patients jaundice is absent, but this is rare. The differential diagnosis from serum hepatitis can only be made on the history, and patients who received transfusions or injections in the 6 months preceding the onset of jaundice may well have obtained their infection in this way. The diagnosis is usually easy and the patient makes an uneventful recovery. At the height of the illness the jaundice often becomes completely obstructive in type and urobilin disappears from the urine. Improvement is heralded by its return.

In some cases acute liver failure develops and ominous signs of this complication are a sudden considerable reduction in the size of the liver, widespread bleeding, and the appearance of 'foetor hepaticus'. The outcome is nearly always fatal. Also rarely, hepatitis may enter a subacute phase and the patient may die in liver failure after some months. Patients may recover from subacute hepatitis but may develop cirrhosis at a later stage. Those entering this subacute phase never recover completely from the acute illness, and if there is a relapse in a patient who has had good health for some months, either a fresh infection has occurred or the diagnosis is incorrect.

It is important to realize that even with complete recovery it is common for the flocculation tests to remain abnormal for many months and often for a year. This has no significance; the so-called 'post-hepatitis syndrome' is no more than post-infection debility and is far commoner than subacute hepatitis. The patient should be reassurred after liver disease has been excluded.

Drugs may cause jaundice, which must be distinguished from infective hepatitis and may be haemolytic, hepatocellular or obstructive in type. Iproniazid (marsilid) is the most important drug amongst those which cause hepatocellular jaundice but it has also been ascribed to PAS, sulphonamides and various chlorinated hydrocarbons. The pathological picture is identical with that of infective hepatitis[31] and the clinical picture is very variable according to the extent of the liver-cell necrosis.[32] In severe cases there is deep jaundice and the patient may die in hepatic coma. Complete recovery occurs in milder cases. The results of corticosteroid therapy are still to be assessed.

Obstructive jaundice may be caused by chlorpromazine (largactil), methyl testosterone, norethandrolone (nilevar), thiouracil, and arsphenamine. While many patients receiving norethandrolone have excessive bromsulphalein retention,[33] only a small percentage develop jaundice. It is estimated that 1 - 2% of patients given chlorpromazine for 1 week develop jaundice. There is a latent period of 1 - 4 weeks followed by fever, anorexia, vomiting, abdominal pain, skin rash, and severe pruritus. Eosinophilia occurs in the early stages. Biochemically these patients characteristically show an obstructive jaundice with a high serum bilirubin, raised serum alkaline phosphatase (often higher than 30 King-Armstrong units, as it is also in mechanical obstruction, e.g. by stone), raised serum cholesterol, no bile in the stools, and no urobilin but a large amount of bile in the urine. The majority of patients recover completely in about 4 weeks. An occasional patient remains jaundiced for months and rarely a patient may succumb from this complication of chlorpromazine therapy. Pre-existing liver disease does not predispose to chlorpromazine jaundice.[6] The incidence of hepatic involvement is not related to the size of the dose or for the period for which it is taken.

The differential diagnosis between acute heptatitis with obstructive jaundice and mechanical obstructive jaundice may be very difficult. In differentiating between hepatitis and jaundice due to stone it must not be forgotten that older patients are no more exempt from developing hepatitis than younger people are from having stones. Severe abdominal pain suggests biliary colic but may also occur in hepatitis. Gall-stones in the common bile-duct may be painless. Rigors are characteristic of ascending cholangitis complicating mechanical obstruction but may occasionally occur in the early stages of hepatitis. An enlarged smooth liver commonly occurs in mechanical obstruction and even splenomegaly has been described. Nodules in the liver suggest intrahepatic obstruction by carcinoma, and a palpable gall-bladder indicates carcinoma of the ampulla of Vater or head of the pancreas. Carcinomatous masses may be felt in the pouch of Douglas. Straight X-ray of the abdomen may reveal gall-stones, 10% of which are radio-opaque. Previous biliary surgery suggests the possibility of traumatic stricture of the common bile-duct. It is clear that diagnosis may be difficult and the probabilities have to be weighed carefully in every case. If in doubt about the diagnosis the clinician is advised to observe the patient for 3 weeks before advising

laparotomy. During this period most patients with infective hepatitis will show improvement, underlying cirrhosis usually becomes apparent, and no irreversible damage will have been done to the liver. Liver biopsy is sometimes helpful but often inconclusive. ACTH (40 units twice a day for 4 days) or prednisone (40 - 60 mg. a day for 1 week) may be of diagnostic use.[6,37] A rapid fall in the serum bilirubin of over 70% of the previous level is strongly suggestive of hepatocellular jaundice and there is usually a lesser fall in obstructive jaundice due to gall-stones. If the clinician is still in doubt at the end of 3 weeks, then a laparotomy is performed and at operation not only must the common bile-duct be palpated and if necessary explored, but also an operative cholangiogram must be done, as must an operative liver biopsy. If operative cholangiograms are not done then small common-duct stones will pass undetected and the patient will have to be submitted to further operations needlessly.

Treatment of Hepatitis

It would seem wise to insist on bed rest in the treatment of patients with hepatitis who stay at home and are not admitted to hospital. It has been pointed out that the good results claimed for treatment with early ambulation were obtained in young servicemen during a mild epidemic.[34,35] Patients in hospital may be allowed up for a few hours each day if they have no symptoms. Strict bed rest is enforced if symptoms recur. Fuller activities are not allowed until the serum-bilirubin level reaches 1·5 mg.%. Patients should be allowed to choose their diet and should be encouraged to have one rich in protein as soon as possible. Antibiotics have no part to play in treatment. Corticosteroids induce a rapid remission clinically and biochemically but if treatment is stopped too early relapse occurs. As in the average case the prognosis is good and the illness short, these steroids should not be used as a routine. They may be used in patients with severe obstructive features and will result in a fall in the serum bilirubin but there is still no evidence that they shorten the duration of the illness. In the rare case of acute liver failure protein by mouth must be stopped and the regime for the treatment of hepatic coma instituted. Corticosteroids are given as a desperate measure.[36] The prognosis is very poor when this rare complication occurs.

Pruritus may present a problem in treatment. The mild pruritus due to hepatitis is best treated with calamine lotion or antihistaminic drugs. Methyl testosterone, norethandrolone or corticosteroids should be reserved for the pruritus of the more prolonged cases of severe obstructive jaundice.

III. SUPPLEMENTARY

TRANSAMINASES

The normal value for glutamic oxalacetic transaminase in the serum is 5 - 40 units; this value may be increased by 20 to 500 times in acute hepatitis.[37] The normal value for serum glutamic pyruvic transaminase is 7 - 23 units and this is also greatly increased in acute hepatitis. The clinical severity parallels the increase in the serum levels of these enzymes to a certain extent. Their greatest value lies in the early diagnosis of infective hepatitis and in detecting the development of subacute hepatitis or relapses. Patients with decompensated cirrhosis show higher serum levels than those with compensated disease.[38] Merrill *et al.*[39] have related the rise in the serum-enzyme level to the amount of cellular necrosis found on liver biopsy, and this has been confirmed by other workers.[40] It has also been shown that there is a corresponding decrease in the liver content of these enzymes. They have not proved of value in the differential diagnosis of obstructive jaundice, for serum levels may be increased to a certain extent even in posthepatic obstruction. This is due to the focal hepatic necrosis that commonly occurs in this condition. It is well known that serum values for these enzymes may also be increased after myocardial infarction and in muscular diseases. In summary, therefore, it may be said that these enzymes may be present in increased amounts in the serum when there is liver-cell necrosis.

BILE PIGMENTS

The advances in this field are due to the application of reverse-phase partition-chromatography.[41] By this means the bile pigments have been identified as consisting of haemobilirubin, pigment I, and pigment II. Haemobilirubin is unconjugated and is the pigment which reacts indirectly with the Van den Bergh reagent and is increased in the serum in haemolytic jaundice. In the normal liver haemobilirubin is converted to pigment I by conjugation with one glucuronide molecule; this in turn is converted into pigment II which is conjugated with 2 glucuronide molecules; 80% of bilirubin is excreted as a glucuronide conjugate and 10 - 15% as a conjugated sulphate. Some conjugation may take plase in extrahepatic sites, as has been demonstrated in the hepatectomized animal. In adult haemolytic disease, slight increases in the amount of pigment I and pigment II in the serum are thought to be due to associated hepatic dysfunction. In the normal premature infant, jaundice is probably related to a deficiency of at least 2 enzymes—glucuronyl transferase and uridine diphosphate glucuronic acid dehydrogenase, the enzymes necessary for the conjugation of haemobilirubin. In haemolytic disease of the newborn there is a great increase in circulating haemobilirubin, which is toxic to the cells and causes kernicterus. Pigments I and II are non-toxic. In mechanical obstructive jaundice, cirrhosis and hepatitis there is an increase in the serum levels of pigments I and II. In mechanical obstruction to the flow of bile the serum level of pigment II tends to be higher than that of pigment I, while in hepatitis and cirrhosis the reverse is the case. There is a considerable amount of overlapping and so this is of no value in distinguishing between these types of jaundice.

ESSENTIAL HYPERBILIRUBINAEMIA

1. *Gilbert's Disease*

The precise incidence of this disease is not known but it is probably far commoner than is generally thought. The patient usually has no symptoms but jaundice occurs from time to time. The serum bilirubin is usually less than 5 mg.% and is always of the unconjugated (indirect reacting) type. There is no bile in the urine. Liver biopsy is normal. The jaundice may be noted during an examination for an intercurrent illness, and hepatitis may be erroneously diagnosed. The persistence of the jaundice may lead to the diagnosis of subacute hepatitis and cirrhosis and unnecessary invalidism may result. The prognosis is excellent and no treatment is necessary.

2. *Dubin-Johnson Disease*

In this rare disease the patients often have symptoms. Bile is present in the urine and there is an increase of con-

jugated (direct reacting) pigment in the serum. The bromsulphalein test is abnormal. Oral cholecystography reveals a non-functioning gall-bladder, and on liver biopsy the liver is found to be coloured by a coarse brown pigment, though in rare cases there is no pigment.

3. *Crigler-Najjar Disease*

This is a very rare, severe form of Gilbert's disease characterized by kernicterus, mental defect, and death at an early age. It is inherited as a Mendelian dominant.

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TEMPERATURE CHANGES IN CHILDREN DURING GENERAL ANAESTHESIA*†

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The state of anaesthesia depresses and renders inefficient the temperature-regulating mechanisms of the body. Placed in conditions of high ambient temperature with which its deranged compensatory mechanisms cannot cope, the body temperature of the anaesthetized patient has been shown to rise. This is especially so in children in whom there are the additional factors of small body mass, high internal production, and immature regulatory mechanisms. The foregoing and the evil effects of hyperpyrexia in the anaesthetic state—notably convulsions and death—are well documented.[1-4]

The air conditioning of operating theatres—originally recommended by Huntington in 1920[4]—is a logical solution to the problem of heat accumulation during anaesthesia and is now widely accepted in the normal design of operating theatres. There are, however, no published observations on the body temperatures of subjects anaesthetized in such surroundings.

The advent of halothane, which appears to cause a more profound disturbance of the body-heat regulatory mechanism than does ether, the agent most commonly used in the papers referred to, provided a further stimulus to this study.

We report here on a statistical analysis of observations of body temperature made on 248 infants and children undergoing general anaesthesia and surgery.

The operating theatre. The operating theatre in which these observations were made is air conditioned, the average temperature range being 70° - 75° F., with a relative humidity of between 70 - 75%.

Anaesthesia

1. Halothane group: 166 cases were anaesthetized with halothane, nitrous oxide and oxygen.

2. Miscellaneous group: 82 cases were anaesthetized with nitrous oxide and oxygen and ether, and/or cyclopropane or trilene. Of these the majority were given ether.

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† Abstract of a paper presented at Research Forum, University of Cape Town, 17 February 1960.

RESULTS

1. There was a mean fall in temperature during general anaesthesia. This was 2·1° F. in the group of cases anaesthetized with halothane and 1·0° F. in a group aneasthetized with other anaesthetics.

2. The benefit of the air conditioning of the operating theatre is stressed. Over the observed range of theatre temperatures there was a positive relation between this and the patient's change in temperature. In this range of theatre temperature the comparatively narrow range of relative humidity observed had no bearing on the change in temperature of the patient.

3. Small infants (less than 20 lb.) cool to a significantly greater extent than the larger and this fall is progressive with time. Mean fall in temperature in children of under 10 lb., 10 - 20 lb. and 20 - 50 lb. weight was 4·3° F., 2·3° F., and 1·5° F. respectively. The larger infants (more than 20 lb.), after an initial rapid fall in temperature (especially with the use of halothane), attain a relatively static temperature. Similar conclusions follow an analysis of the fall in temperature in relation to the patient's surface area.

4. The fall in temperature is related to the site of operation; the greater the exposure, especially of viscera, the greater the fall in temperature.

5. The pre-operative presence of pyrexia had no bearing on the change in temperature during anaesthesia.

6. The transfusion of blood led to an increased fall in temperature.

7. The mean fall in temperature in neonates was 5·9° F. When hot-water bottles at 101° F. were placed under the patient, the mean fall was 3·2° F.

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VAN DIE REDAKSIE : EDITORIAL

DIE WANVERDELING VAN GENEESHERE

Gedurende sy onlangse ses-maandelikse sitting in Kaapstad, is die probleem van die ‚wanverdeling' van dokters in Suid-Afrika weer eens deur die Suid-Afrikaanse Geneeskundige en Tandheelkundige Raad, op voorstel van dr. H. Grant-Whyte, van Durban, bespreek, met spesiale verwysing na die verhouding tussen algemene praktisyns en spesialiste, en met verwysing na die verspreiding van dokters in stedelike en plattelandse gebiede en in Blanke en Naturellegebiede.

Wat die verhouding tussen algemene praktisyns betref, lyk dit of die posisie gestadig verswak. Volgens die amptelike syfers wat aan die einde van 1958 verstrek is deur die Geneeskundige en Tandheelkundige Raad, was daar toe 1,433 geregistreerde spesialiste en 7,549 algemene praktisyns in die land—'n verhouding van ongeveer 1 : 5. Volgens die jongste beskikbare syfers het hierdie verhouding nou gedaal tot ongeveer 1 : 4.

Op grond van die mening en ondervinding van praktiserende dokters self, is hierdie verhouding ongewens en ongesond. Dr. A. W. S. Sichel, 'n lid van die Geneeskundige en Tandheelkundige Raad, het byvoorbeeld gesê dat ons oorbevolk word ten opsigte van spesialiste en dat hierdie toestand 'n baie ernstige probleem skep. En dr. G. F. C. Troskie, 'n lid van die Federale Raad van die Mediese Vereniging van Suid-Afrika, het onlangs in sy afskeidsrede as aftredende President van die Tak Oranje-Vrystaat en Basoetoland, die volgende weloorwoë verklaring gemaak: ‚Omdat sommige spesialiste nie meer 'n redelike bestaan in die stede kon maak nie, het hulle na die buitesentrums begin gaan waar fasiliteite beskikbaar is en het hulle hulle dienste aan die publiek naby die huis beskikbaar gestel. Hierdie ontwikkeling voorsien nie net in 'n behoefte op die platteland nie, maar verseker ook vir die meerderheid van daardie spesialiste 'n goeie inkomste. Dit het egter die toestand van die stedelike spesialiste kritiek gemaak. Waar die redelike verhouding van spesialiste tot algemene praktisyns op 1 : 12 gestel word, het die spesialiste op die plattelandse dorpe in sommige gevalle die verhouding op hulself gekonsentreer tot 1 : 15 en 1 : 20, terwyl die verhouding ten opsigte van die stedelinge gesny is in sommige gevalle tot 1 : 2; dit is in werklikheid 'n belaglike syfer.'

As voorbeelde van ander praktiese aspekte van die probleem van die verspreiding en voorsiening van dokters, kan ons die volgende noem: Dr. L. O. Vercueil, van die Rand, het verwys na die onmoontlike toestand wat vir baie praktisyns ontstaan het omdat dit feitlik volstrek onmoontlik geword het om die aflosdienste van 'n *locum tenens* te kry. Prof. E. H. Cluver, Dekaan van die Fakulteit van Geneeskunde van die Universiteit van die Witwatersrand, het aangetoon dat werklik bevredigende mediese dienste nie deur ongeveer agt duisend dokters aan nagenoeg vyftien miljoen persone ('n dokter-pasiënt verhouding van 1 : 1,800) gelewer kan word nie.

Prof. I. Gordon, Dekaan van die Fakulteit van Geneeskunde van die Universiteit van Natal, het die probleem van die wanverdeling van dokters bespreek veral met betrekking tot die voorsiening van geneeskundige dienste aan die nie-Blankes van Natal. Hy meen dat die algemene gesondheidspeil van die nie-Blankes gestadig agteruitgaan omdat daar nie voldoende geneeshere is om hierdie aspek van ons nasionale probleem te behartig nie. Professor Gordon meen dat ons op hierdie gebied te staan gekom het voor 'n akute nasionale noodtoestand.

Alhoewel daar in Suid-Afrika gedurende die afgelope vyftig jaar skouspelagtige vordering gemaak is op verskillende terreine van die mediese dienste, en alhoewel die kwaliteit van die werk wat deur geneeshere gelewer word—wat betref die opleiding van voor- en nagraadse studente, navorsing, en die uitoefening van die mediese praktyk self—goed vergelyk met ooreenkomstige dienste elders in die wêreld, staan ons tog nog voor baie ernstige probleme. *Wat* die spesifieke oplossing is vir die soort probleme wat spruit uit die wanverdeling van dokters aangaande status, die gebied van praktyk, en die verhouding van dokters tot die bevolkingsamestelling en van doktersgroepe tot mekaar, weet ons nie. Maar, alhoewel ons nie weet wat die oplossing is nie, rus die verpligting tog op ons om ernstig en onverpoos na 'n oplossing te soek. Met hierdie doel in gedagte moet ons die besprekings van die Geneeskundige Raad en van die Mediese Vereniging, sowel as die oorwegings van individuele lede van die mediese professie, aanmoedig as tydige en verantwoordelike pogings om die grondslag van die mediese beroep in Suid-Afrika op 'n gesonde en produktiewe vlak te hou. Die Kommissie van ondersoek wat deur die Minister van Gesondheid aangestel is om ondersoek in te stel na die hoë koste van mediese dienste, sal probleme wat spruit uit die wanverdeling van dokters ook in aanmerking neem by hul ondersoek. Ons wil dus 'n beroep doen op almal wat konstruktiewe gedagtes oor hierdie saak het, om hulle gedagtes aan die Kommissie voor te lê.

THE MALDISTRIBUTION OF DOCTORS

Problems arising from the so-called 'maldistribution' of doctors in South Africa were again discussed by the South African Medical and Dental Council at its recent meeting in Cape Town. The discussion was introduced by Dr. H. Grant-Whyte, of Durban, and dealt mainly with such problems as the ration of specialists to general practitioners, and the distribution of doctors in urban and rural areas and in European and non-European areas.

The position regarding the ratio between specialists and general practitioners seems to have been steadily deteriorating. According to the official figures supplied by the Medical Council at the end of 1958, there were 1,433 registered specialists and 7,549 general practitioners in the country—a ratio of approximately 1 : 5. The latest figures suggest that the ratio is at present approximately 1 : 4.

On the submission of practising doctors themselves a ratio such as this is both unsound and undesirable. Dr. A. W. S. Sichel, a member of the Medical Council, stated, for instance, that we are becoming overcrowded with specialists, and that this has created a grave problem. Dr. G. F. C.

Troskie, a member of the Federal Council of the Association, in his valedictory address as retiring President of the Orange Free State and Basutoland Branch, recently stated as his considered opinion that: 'Because some specialists were not able to make a reasonable living in the cities they started going to rural areas where the necessary facilities were available; they therefore made their services available to the public nearer home. This development not only met a definite need in the country, but it also led to a fairly good income for most of these specialists; it precipitated, however, a critical situation for the specialist in the city. A satisfactory ratio between specialists and general practitioners is 1 : 12, and some of these specialists who moved into the country attracted more support from practitioners (in the ratio of 1 : 15 or even 1 : 20). This however, cut down the ratio in some of the urban areas to 1 : 2, which, of course, is a ridiculous situation'.

Examples of other practical aspects of the problem of the distribution and supply of doctors in this country are the following: Dr. L. O. Vercueil, of the Rand, referred to the great difficulty in obtaining the services of a *locum tenens*; and Prof. E. H. Cluver, Dean of the Faculty of Medicine of the University of the Witwatersrand, pointed out that adequate and satisfactory medical services cannot be rendered by eight thousand doctors to a population of fifteen million people (a doctor-patient ratio of approximately 1 : 1,800).

Prof. I. Gordon, Dean of the Faculty of Medicine of the University of Natal, discussed the problem of maldistribution of doctors with special reference to the provision of medical services to the non-White peoples of Natal. He stated that the general level of the health of non-Whites has been steadily deteriorating because there are insufficient practitioners to handle this part of our national problem. Professor Gordon feels that we are, in this respect, facing a national emergency.

In spite of the fact, therefore, that we have in this country seen spectacular advances in all fields of medicine over the past fifty years; and in spite of the fact that the quality of medical work in general, including undergraduate and postgraduate training, research, and the practice of medicine compares favourably with the services available elsewhere in the world, we are nevertheless facing a very serious problem. We do not know *what* the solution to the problem of maldistribution of doctors is, particularly in regard to their status, the locality in which they practise, and the ratio between doctors and the rest of the community and between groups of doctors themselves; but we do know that we are under an obligation to try to find a solution. We must, therefore, accept and encourage the efforts made by the Medical Council and the Association, as well as by individual practitioners, as timely and responsible attempts to ensure that medical practice in this country will remain on a sound and productive level. The Commission, which has recently been appointed by the Minister of Health to investigate the factors responsible for the high cost of medical services, will probably include in their investigation problems arising from the maldistribution of doctors. We, therefore, appeal to those who have constructive views on this subject to submit them to the Commission.

THE AGE OF THE MENARCHE AND OF THE MENOPAUSE IN WHITE SOUTH AFRICAN WOMEN AND CERTAIN FACTORS INFLUENCING THESE TIMES

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In several countries investigations have been carried out to determine the average age of the menarche and of the menopause.[1,2,7,9-13,16-18,23-25] As long ago as 1862 Tilt[22] stated that women in tropical climates reached the menarche earlier than those living in temperate and cold countries. However, other investigators[5,13] have found the reverse to be the case; and sexual maturity is said to be retarded in animals kept in a hot, moist atmosphere.[15] Shaw[20] states that amongst the Esquimaux the average age of puberty is 23 years; Young,[26] on the other hand, maintains that the menarche is early in these people. Emily Kark[9,10] attributes an influence to social and economic conditions; investigating Indian girls in Durban, South Africa, she found that the menarche was significantly earlier in the well-to-do than in those less privileged.

It has often been stated that the earlier the menarche occurs, the later the menopause; this belief is probably based on clinical impressions, or on an idea that the short-lived ovary begins to function late and peters out early. But this has not been established. The correlation of the age of the menopause with the marital status and the number of pregnancies has also not been investigated.

It is obviously important to know what is normal and abnormal in these respects for women of different races in this country, not only from the point of view of assessing such deviations as precocious or delayed puberty or menopause, but also because of the increasing evidence that women with cancer of the uterus,[3,4,19,23] and women with 'pituitary-type' diabetes mellitus,[1,14,23] cease menstruating later than normal.

In view of these gaps in our knowledge and the conflicting reports in the literature, an investigation was carried out on a large series of White women in the Cape Province to determine (*a*) the age of the menarche, (*b*) the age of the menopause, (*c*) whether there is a correlation between the two ages in the same women, (*d*) whether the number of pregnancies and the marital status affect the menopausal age, and (*e*) whether the age of the menopause is different in women who develop cancer of the endometrium, cancer of the cervix, or diabetes mellitus.

Method

For the purpose of this analysis 1,000 random White women, who had already reached the menopause, where interrogated. These comprised White patients attending the medical and the casualty departments of the Groote Schuur Hospital, Cape Town, some of their visitors, and also patients seen at the gynaecological out-patient department for conditions which would obviously not affect menstrual function

(discharges, prolapse, etc.). In addition to these 1,000 women, who served as controls, the following groups of White patients were interrogated along the same lines, or the information was obtained from the records of the hospital:

1. 200 consecutive cases of carcinoma of the cervix.
2. 100 consecutive cases of carcinoma of the body of the uterus.
3. 100 consecutive post-menopausal women attending the diabetic clinic of the hospital.

A similar investigation was attempted on Bantu (African) women, but so far sufficient reliable data have not been obtained.

All patients who were uncertain about the age of the menarche or menopause, were excluded; likewise, only those who had lived in the Cape Province for most of their lives were included. The women were questioned about the age of the menarche, the age of the menopause, their marital status, and also about the number of children and abortions. Although in some cases menstruation ceased abruptly, there was more commonly an alteration in the cycle at the climacteric, with oligomenorrhoea and bouts of amenorrhoea—for this analysis the menopause was regarded as having occurred only when a year had elapsed with freedom from bleeding; any bleeding thereafter was recorded as post-menopausal bleeding. In cases where the age was given in terms of years and months, the nearest year was taken; that is to say, below 6 months was placed in the category of the preceding year and above 6 months in the subsequent year.

Age at Menarche

Fig. 1 shows the age of the menarche of the 1,000 control women; the average age was 14·6 years. This is slightly older than the figure given by most authors in other

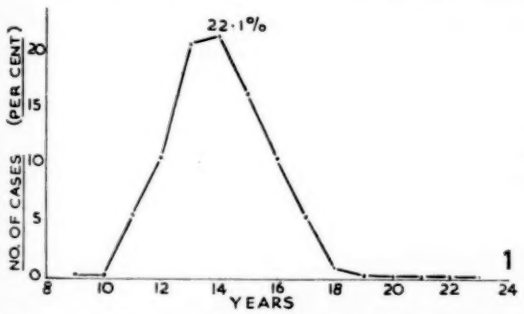

Fig. 1. Age at menarche (White women). Average age 14·6 years. Peak age 14 years. Before 13 years 17·8%. After 14 years 38·4%.

countries, who placed the average age between 13 and 14 years.[2,5,7,9-11,13,16-18,21 25] However, the peak ages are 13 and 14 years (together 43·8%). The detailed ages are tabulated in Table I. The ages ranged from 9 to 23 years; 17·8% started menstruating before 13 years and 38·4% after 14 years, so that on this basis a later menarche was more than twice as common as an earlier one.

Age at Menopause

The ages of the 1,000 women at the menopause is shown in Fig. 2. The average age of the menopause was 48·7 years, but there is a striking peak (17·9% of the total) at 50 years.

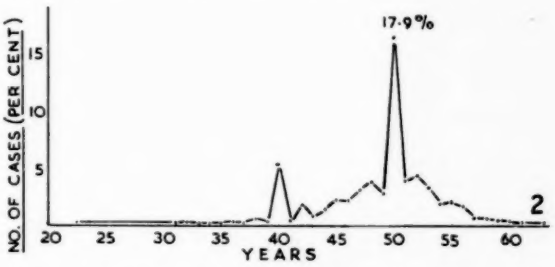

Fig. 2. Age at menopause (White women). Average age 48·7 years. Peak age 50 years. Before 50 years 45·2%. At 50 years 17·9%. After 50 years 36·9%.

The details are listed in Table II; 36·9% continued to menstruate after the age of 50 years (7% after the age of 55 years) and in 45·2% the menopause occurred before the age of 50 years. (13·9% were aged 40–45 years when the menopause set in, 2·9% 35–40 years, and 1% below the age of 35 years.)

Although the peak incidence is at exactly the same age (50 years) as that found by other authors,[23] yet all the evidence shows that *the menopause tends to occur later in South African women than in women in other countries* (Table III). Thus the Medical Women's Federation investigation[12] showed that of 966 women, 71% ceased menstruating before 50 years and 29% thereafter. Of 536 patients,[23] Way found that 65% ceased to menstruate before 50 years, and 35% thereafter. The figures for South African women, by comparison, are 45·2% and 54·8%.

Age at Menarche in Relationship to Age at Menopause

Table I shows the ages of the menarche and the average age of the menopause in each group. This indicates that *the age of the menarche does not appear to have any significant bearing on the age of the menopause.* A more detailed analysis of the women who started menstruating unusually early and unusually late also casts considerable doubt on the idea that a late menarche is followed by an early menopause and an early menarche by a late menopause. Of the 211 cases who began menstruating at 16 years or later, all except 8 had a menopause which was of average age or even late. What is more, of these 8, the menopause was not particularly early (3 at 36 years and 1 at 34 years,) except in 3 women, who ended their menstrual life at 32 years, 31 years and 23 years respectively. Again, Table I shows that those who began menstruating early did not have a late menopause; of the 3 who had the menarche at 10 years, the menopause was at 47 years, 45 years and 38 years respectively, while those who began at 9 years ended at 38, 50 and 53 years respectively.

Further evidence of the lack of association between the menarchal and menopausal ages is furnished by Table II. Of the 10 women who reached the menopause under the age of 35 years, only 1 had the menarche late, i.e. at 17 years, the others having been 15 years or younger when menstrual function began.

Marital Status and Age at Menopause

Amongst the 1,000 women there were 70 unmarried ones. Their ages at menopause are shown in Table IV. The peak age is again 50 years, and this is striking. The percentage of women who had the menopause before 50 years and later (45·7% and 54·3% respectively) is little different from the control group (see Table IX for comparisons).

Number of Pregnancies and Age at Menopause

There were 125 women who had never borne live children when they reached the end of their reproductive years. The ages of the menopause in this group are shown in Table V. Of these, 55·2% reached the menopause before 50 years of age. This indicates that women who have never borne live children tend to have an earlier menopause than women who have had children (see Table II).

An interesting point emerges from this study. Of the 930 married women who had been through their entire reproductive lives, 51 had never conceived. *Thus the incidence of sterile marriages in this series was 5·5%, which is much lower than the figure given for England*—10%[21] *or* 11·7%[8] *and for America*—12%.[6]

Carcinoma of Body of Uterus and Age at Menopause

The 100 cases of carcinoma of the body of the uterus who were post-menopausal were analysed separately. The ages of the menopause are shown in Table VI. Only 26% ceased menstruating before the age of 50 years, whereas 30% were 50 years of age and 44% over 50 years. Comparing this with the figures for the control group (45·2%, 17·9% and 36·9% respectively) *the menopause is seen to occur later in women who subsequently develop carcinoma of the body of the uterus.* The comparisons are made in Table IX.

Carcinoma of Cervix and Age at Menopause

The ages of the menopause in 200 cases of carcinoma of the cervix are set out in Table VI. The percentages who reached the menopause before, at and after 50 years of age were 38%, 19% and 43% respectively. This indicates a *slightly later menopausal age* than in control women, but this feature is not so striking as in cases of carcinoma of the body of the uterus (see Table IX).

Age at Menopause in Diabetes Mellitus

Of 100 consecutive post-menopausal 'pituitary-type' diabetic patients seen at the diabetic clinic, as shown in Table VIII, 39% ceased menstruating before the age of 50 years, 15% at 50 years and 46% after 50 years of age. The diabetic, then, tends to have a later menopause than the normal woman. This phenomenon is not so marked as in cases of carcinoma of the body of the uterus; the tendency is about the same as in cases of carcinoma of the cervix (see Table IX).

SUMMARY AND CONCLUSIONS

1. Information on the average age at the menarche and the menopause in South African women of different races is defective. Likewise the relationship of the age at the menarche to the age at the menopause has not been ascertained in any country; nor has it been established whether the marital status and number of pregnancies affect the age of the menopause.

2. In view of these gaps in our knowledge 1,000 White South African women were investigated. In addition, 100 cases of carcinoma of the body of the uterus, 200 cases of carcinoma of the cervix and 100 diabetic patients (all White) were studied to ascertain whether the menopausal ages of these patients differ from those of the control group. Similar investigations on Bantu African women were tried, but sufficient accurate data have not yet been obtained.

3. The menopause tends to occur later in South African women than in women in other countries. The average age is 48·7 years, but the peak incidence (17·9%) is at 50 years; 45·2% reach menopausal age before 50 years, 17·9% at 50 years and 37·9% after 50 years.

4. The age of the menarche differs little in South African women from that of women in most other parts of the world. If anything the menarche is slightly later in this country. The average age is 14·6 years. On the basis that an age of 13 or 14 is average, a late menarche (38·4% after 14 years) is more than twice as common as an early one (17·8% before 13 years).

5. The idea that the earlier the menarche occurs the later the menopause, and the later the menarche the earlier the menopause, is not supported by the facts brought out in this investigation.

6. The marital status does not appear to affect the age of the menopause to any great extent.

7. Women who have never conceived, however, tend to reach the menopause earlier than those who have had children or abortions.

8. Women who develop carcinoma of the body of the uterus in the post-menopausal era tend to have a later menopause than women in a control group; the same phenomenon was observed in a series of cases of carcinoma of the cervix and 'pituitary-type' diabetes mellitus, but not to as marked a degree as in patients with endometrial carcinoma.

9. The proportion of married South African White women who pass through their whole reproductive life and remain sterile is 5·5%. This is much lower than the proportion in England and America.

I should like to express my thanks to Dr. J. G. Burger, Superintendent of the Groote Schuur Hospital, who kindly granted permission to publish data about patients attending the hospital. I am indebted to Prof. James T. Louw for encouragement and helpful criticism, and to Prof. E. C. Crichton for reading and making suggestions on the manuscript. Dr. W. P. U. Jackson kindly allowed us to interrogate patients attending the diabetic clinic of the Groote Schuur Hospital. Mrs. C. Hall collected the records of the cancer patients and Sister T. Fox and her staff at the out-patient department were of considerable help in the collection of data from out-patients. All this is gratefully acknowledged.

TABLE I. AGE OF MENARCHE AND AVERAGE AGE OF MENOPAUSE

No. of Cases	*Age of Menarche*	*Average Age of Menopause*
3	9	47
3	10	43·3
51	11	49·8
121	12	48·6
217	13	48·6
221	14	48·5
173	15	48·9
117	16	49·0
61	17	49·7
23	18	48·3
5	19	49·4
2	20	47
1	21	34
1	22	50
1	23	52
1,000	14·6 (average)	48·7 (average)

178 (17·8%) before 13 years
384 (38·4%) after 14 years

TABLE II. AGE OF MENOPAUSE AND AVERAGE AGE OF MENARCHE

No. of Cases	*Age of Menopause*	*Average Age of Menarche*
3	23	13 (b)
1	31	17 (a)
3	32	14 (c)
1	33	13 (a)
2	34	15 (d)
1	35	14 (a)
5	36	16 (e)
4	37	14·3 (f)
10	38	12·7
9	39	13·3
52	40	14·4
7	41	13·9
35	42	11·8
16	43	13·8
29	44	14·5
41	45	13·7
41	46	13·8
60	47	14·0
75	48	14·2
57	49	13·8
179	50	14·2
74	51	14·3
83	52	13·9
64	53	14·3
38	54	14·4
40	55	14·1
31	56	14·4
13	57	14·7
11	58	13·7
6	59	16 (g)
6	60	13·8 (h)
2	61	12·5
1	63	16

452 (45·2%) before 50 years
179 (17·9%) at 50 years
369 (36·9%) after 50 years

(a) 1 case only (b) 11,13,15
(c) 12, 13, 17 (d) 15, 15
(e) 13, 15, 16, 18, 18
(f) 13, 14, 14, 16
(g) 13, 15, 16, 17, 17, 18
(h) 11, 12, 15, 15, 15, 15

TABLE III. COMPARISON OF MENOPAUSAL AGES IN SOUTH AFRICAN WOMEN AND WOMEN IN OTHER COUNTRIES

	Before 50 years	*50 years and after*
This series (*a*)	45·2%	54·8%
Way[23] (*b*)	65%	35%
MWF[12] (*c*)	71%	29%

(*a*) 1,000 women. (*b*) 536 women. (*c*) Medical Women's Federation, 966 women

TABLE IV. UNMARRIED WOMEN

Age of Menopause	*No. of Cases*	%
36	1	1·4
37	1	1·4
38	2	2·9
39	0	0
40	3	4·3
41	0	0
42	1	1·4
43	0	0
44	4	5·7
45	4	5·7
46	4	5·7
47	6	8·6
48	3	4·3
49	3	4·3
50	17	24·3
51	9	12·9
52	3	4·3
53	3	4·3
54	1	1·4
55	2	2·9
56	2	2·9
57	0	0
58	1	1·4
	70	100

Before 50 years 45·7%
50 years and after 54·3%

TABLE V. MARRIED WOMEN WHO NEVER BORE LIVE CHILDREN

Age of Menopause	*No. of Cases*	%
23	1	0·8
32	1	0·8
33	0	0
34	1	0·8
35	0	0
36	3	2·4
37	1	0·8
38	2	1·6
39	1	0·8
40	10	8·0
41	1	0·8
42	2	1·6
43	2	1·6
44	5	4·0
45	10	8·0
46	8	6·4
47	9	7·2
48	4	3·2
49	8	6·4
50	19	15·2
51	11	8·8
52	9	7·2
53	5	4·0
54	1	0·8
55	3	2·4
56	3	2·4
57	1	0·8
58	2	1·6
59	0	0
60	1	0·8
61	1	0·8
	125	100·0

Before 50 years 55·2%
50 years and later 44·8%
Incidence of sterility in 930 married women 5·5%

TABLE VI. CARCINOMA OF THE BODY OF THE UTERUS (100 CASES)

Age of Menopause	*No. of Cases*
45	4
46	6
47	8
48	3
49	5
50	30
51	7
52	13
53	8
54	6
55	4
56	2
62	3
63	1

Before 50 years 26%
At 50 years 30%
After 50 years 44%
50 years and later 74%

TABLE VII. CARCINOMA OF THE CERVIX (200 CASES)

Age of Menopause	*No. of Cases*	%
35	2	1
40	6	3
41	2	1
42	4	2
43	4	2
44	10	5
45	6	3
46	6	3
47	8	4
48	18	9
49	10	5
50	38	19
51	14	7
52	18	9
53	22	11
54	10	5
55	10	5
56	4	2
57	2	1
58	2	1
59	2	1
60	0	0
61	2	1

Before 50 years 38%
At 50 years 19%
After 50 years 43%
50 years and later 62%

TABLE VIII. DIABETES MELLITUS (100 CASES)

Age of Menopause	*No. of Cases*
37	1
38	2
39	1
40	3
41	2
42	6
43	3
44	4
45	1
46	1
47	8
48	5
49	2
50	15
51	13
52	7
53	8
54	5
55	2
56	3
57	4
58	2
59	2
60	0

Before 50 years 39%
At 50 years 15%
After 50 years 46%

TABLE IX. AGE OF MENOPAUSE IN CONTROL AND OTHER GROUPS

	Before 50 years	*50 years and later*
Control series (1,000 women)	45·2%	54·8%
Unmarried (70 women)	45·7%	54·3%
Women who had never been pregnant (125 women)	55·2%	44·8%
Carcinoma of body of uterus (100 cases)	26%	74%
Carcinoma of cervix (200 cases) ..	38%	62%
Diabetes mellitus (100 cases)	39%	61%

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ARTIFICIAL INSEMINATION*

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For some years now this subject has been in the public eye and every so often it captures the attention of the lay press. It is a subject which certainly deserves to be thought about earnestly and to be widely discussed, for the opinion of every thinking person is important and relevant. It is not a matter for doctors, clerics and lawyers alone, although they can all give essential guidance. It is also a matter of the heart—is this thing right or is it wrong? We all commiserate and would like to help the childless couple, but the question arises whether this remedy may not possibly be worse than the ailment? Every intelligent man and woman must decide. What follows are the random observations of a gynaecologist.

History

In old Jewish literature there appear to be several oblique references to the possibility of artificial insemination.[1, 2] However, there is no real evidence that AI as we know it was ever practised in those olden times; and artificial insemination with a donor's semen (AID) is certainly rejected by the Jewish religion today.

It is said that in the 2nd century Rabbi ben Zoma debated the question whether a high priest, who by law was allowed to marry only a virgin, could in fact marry a pregnant one! He considered the possibility amongst others that such a pregnancy could have resulted not by ordinary sexual intercourse but by a fortuitous conception. He decided that a virgin who was with child in this particular way was innocent and could therefore become the wife of a high priest.[2]

In the 13th century Rabbi Peretz ben Elijah, of Corbeil in France, bade women beware of lying 'on linen' on which a man other than their husbands had lain lest they become pregnant. If a woman became pregnant in this way the Rabbi decreed that the child should not be regarded as the product of an adulterous union.[2]

According to an old Arab document of the 14th century an inhabitant of the town of Darfur who owned a mare introduced a wad of wool into the genitals and left it there for a day. At night he made his way into the camp of a hostile tribe, who had an excellent stallion, and held the wool under the stallion's nostrils whereupon the horse came into heat and ejaculated. The semen was collected and without delay the mare was successfully inseminated—for she subsequently came into foal.[3]

Another legend of the 14th century has it that an Arab sheikh, who was at war with a tribe who had superior horses, sent his men into the enemy camp to fertilize their mares with the semen of an inferior stallion.[3]

Don Pinchom, a monk in the Abbey of Reame in the 15th century, is credited with the experimental fertilization of fish. In 1780 or thereabouts Spallanzani successfully fertilized fish, an insect, a frog and a dog, while approximately 10 years later the inevitable John Hunter first recorded artificial insemination in the human with the husband's semen (AIH). Marion Sims in 1866 was successful in America with AIH. Other 19th-century practitioners of AIH included Harley in England, Girault and Gautier in France, and Mantegazza in Italy.[3]

The first publication on AID appeared in the *Medical World* (New York) of April 1909, where Hard reports that AID was performed by Professor Pancoast at Philadelphia in 1884.[4]

Indications

AID should never be forced upon a couple and certainly not if the marriage is an unhappy one. As a Dutch writer recently put it, 'Artificiële inseminatie bedoele nooit een kapot huwelijk op te lappen'.[5]

The usual indications are the following:

1. An infertile husband (the commonest).
2. Hereditary disease on the husband's side.
3. Rhesus incompatibility which has already resulted in repeated stillbirths.
4. Repeated miscarriages in the presence of a high percentage of abnormal spermatozoa.
5. Repeated malformed children.

Medical Preliminaries

A complete investigation of the couple with regard to infertility must be carried out.

* A paper read at a symposium on *AID* at a meeting of the Cape Western Branch (M.A.S.A.), Cape Town, 31 July 1959

The husband. The investigation of the husband is usually undertaken by a urologist. His medical history must be gone into and a complete physical examination and semen analysis carried out. It has been stated by some authorities that on the presumption that the fact that the child is an AID child is to remain a secret the husband's ABO blood group must be known so that it may be arranged that the donor's blood group shall be the same as the husband's lest future blood-group tests should lead to disclosure or dispute. But since also the M and N, Rhesus, Duffy, Kell and other factors are used in cases of disputed parentage it seems unrealistic to try to find a donor whose blood group is such that in any future litigation the paternity of the husband could not be disproved. At a practical level therefore I think it rather pointless to limit the choice of a donor in this way.

The wife. Before artificial insemination is carried out it must be shown that the wife is normally fertile. The gynaecologist takes a full history. He carries out a general physical examination and, of course, pays particular attention to the pelvic organs. He then establishes the patency of the Fallopian tubes by insufflation or salpingogram. The histology of an endometrial biopsy in the second half of the menstrual cycle, aided by a study of the cervical mucus and a basal temperature chart, will establish whether ovulation is taking place and when it occurs. Histological examination and culture of the endometrium will also aid in the detection of a possible tuberculous endometritis, a condition relatively common in the infertile woman. It is important to ascertain her Rhesus blood group, because this should be identical with that of any prospective donor if she is Rhesus negative.

Selection of a Donor

I do not think that a donor should be paid for his services. He should be under 40 years of age and should himself be married with two healthy children. He should not be a relation of the couple. He should be a man of good character and of the same race, religion, background and emotional make-up as the husband. His physical appearance, stature and colouring should as far as possible be similar to those of the husband. The donor's general health must be good and there should be no history of epilepsy, psychosis or alcoholism. His family history should be clear. His Wassermann reaction must be negative, while his Rh grouping should be the same as that of the wife if she is Rhesus negative. Finally his semen must be normally fertile and his wife must know and agree that he acts as a donor.

On the question whether a semen bank should be operated or not, the following disadvantages of such a bank may be mentioned:[6]

1. The doctor never sees the donor.
2. Secrecy is less certain.
3. The semen has to be kept for a longer time before insemination.
4. The running and maintenance of the bank will certainly add much to the expense.
5. An organization such as this brings with it the greater risk of mistakes.
6. It may be difficult to find the same donor for a repeat insemination.
7. It is difficult to record successful insemination (i.e. the name of the donor) without sacrificing anonymity and secrecy.

Legal Preliminaries

Eight people are involved, viz. (*a*) the donor, his wife, and the witness to their signatures of consent, (*b*) the husband and wife and the witness to their signatures of consent, (*c*) the doctor, and (*d*) the child.

The legal implications must be explained to everybody concerned and each one of the couples concerned must sign a suitable consent form. The legal validity of such consent has been questioned.

There must be complete secrecy about everything. The donor must not know who the recipient is and *vice versa.* Neither must the donor know whether the artificial insemination was successful or not.

Technique of Insemination

This is very simple. The time of ovulation is determined from a study of the basal temperature chart and the cervical mucus, and insemination is performed within 24 hours of this time.

The semen is collected from the donor by masturbation and should be used within 1½ hours. The patient is placed in the lithotomy position. The semen is drawn up into a dry cool syringe with an intravenous cannula attached. An unlubricated sterile speculum is placed in the vagina. No douching or wiping of the cervix is done and the semen is deposited round the external os. The speculum is withdrawn and the patient allowed to remain lying down for 30 minutes.

Insemination is performed two or three times at the time of ovulation during each menstrual cycle. It is advisable to instruct the couple to have normal intercourse at about this time. Some practitioners advise the mixing of the donor's semen with a little of the husband's if the latter does contain a small number of spermatozoa (where the indication for AID is an infertile husband); fertilization with the husband's spermatozoa is then always a possibility albeit a theoretical one. Insemination is carried out on an average for about 6 months but can of course be continued for longer.

Medical complications. These are few, but presumably pelvic infection could occur if the semen were deposited in the uterus, and the transmission of syphilis or gonorrhoea is certainly possible.

Results. Pregnancy ensues in 50-60% of cases if insemination is carried out for about 6 months, and success rates of 75% have been reported. The abortion rate and stillbirth rate in these pregnancies are no higher than normal, and the number of malformed babies is also no greater than the usual.

Psychological reaction. Practitioners who employ AID are all agreed that when AID has been successful the husband and wife have always been extremely happy and in many instances have returned for another baby. The frightful domestic difficulties and problems which are written about hardly ever arise in practice.

Some Objections that are Raised

(*a*) *Too much power in the hands of the doctor:* It is said that by allowing the practice of AID too much power is placed in the hands of a doctor, who may abuse the power. The answer to this objection is that medical practitioners are entrusted with no less power and responsibility in many fields, and that the profession has shown itself worthy of the trust that is placed in it.

(*b*) *Masturbation.* Objections to this are understandable. Possibly the semen could be collected by coitus interruptus instead, but urologists consider that it is safer to use a masturbation specimen of semen. Many feel that the fundamental moral objection to masturbation disappears if it is done without a feeling of guilt and with the definite object of helping an infertile couple.

(*c*) *Separation of the reproductive from the sexual function.* This again is understandable, but the objection equally applies to contraception, which most people are prepared to practise.

(*d*) *Adoption versus AID.* Adoption may certainly be the solution for many infertile couples, but there will always be the woman with a very strong maternal instinct who will prefer AID; it is an obvious benefit that the mother knows that she herself has conceived and given birth to the child. In adoption the parents of the child are often unknown, whereas in AID the mother at least is known and the donor is most carefully selected. It should also be remembered that the demand for babies to adopt far exceeds the supply—there are just not enough babies to go round.

(*e*) *Marriage of siblings.* This is a possibility, albeit very small, especially in a small community. But of course it also applies to some extent to adoption.

(*f*) *A tantalizing question.* If the wife of a sterile husband is allowed to have a child by AID should the husband of a sterile wife be allowed to produce a child by having AID performed with his semen on another woman (if such can be found!) and then bring the child into the family?

Legal Complications

Although this aspect does not strictly fall within the medical realm one cannot help mentioning a few points.

Adultery. That AID constitutes adultery has been held, for instance, by certain religious authorities and in the South African text-book *Medical Jurisprudence* (Gordon, Turner and Price[7]). Adultery has been defined as 'voluntary sexual intercourse between a married person and a person of the opposite sex, not the other spouse, during marriage'. If one accepts this definition it is difficult to see how AID can be an act of adultery.

Legitimacy of the child. It is generally agreed that in South Africa the child is illegitimate.[7] But this may be impossible to prove when the husband not absolutely sterile has had intercourse with his wife during the same menstrual cycle as when AID was performed or if some of his semen was mixed with that of the donor. One wonders, however, whether the child cannot be legally adopted by the husband and wife.

Registration of the child's birth. If in registration the husband declares that he is the father he is committing a punishable offence.[7] This issue, however, may be subject to the consideration mentioned in the preceding paragraph.

Doubtful or Dangerous Uses of AID

The following contingencies may call for special consideration:

1. The production of an heir from a donor with some particularly outstanding ability.

2. It may be possible now to separate male-producing from female-producing spermatozoa and therefore to use this knowledge to alter the sex ratio in a particular community.

3. AID may be used to reverse the falling birth rate in a particular community or country.

4. By physical or chemical treatment of the spermatozoa, e.g. X-rays, it may be possible to induce certain genetic modifications which can then be propagated by AID.

5. AID may enable a spinster to have a child of her own.

Some of these propositions may seem to be far-fetched but are they really so in this our age of lunar lunacy?

CONCLUSION

It has been said by a wise man that if something must be kept secret it is probably wrong, and I think I feel this way about AID.

I fear that AID and all that goes with it may rock the very foundations upon which our family life and society are based. To me it spells a mockery of marriage and a marriage of mockery. There are a great many difficulties and probably too much is risked by its practice. Perhaps, therefore, AID is better prohibited by law altogether. Such prohibition, however, may drive the practice underground, with even more serious consequences should it then fall into the hands of unqualified practitioners. But if AID is not prohibited by law, then the doctor, the couple concerned, the donor, and the child born after insemination, must be protected by the law in every possible way. The present state of legal uncertainty should not continue.

The selection of couples must of course be done most carefully. The alternatives (remaining childless or adopting a child) and all the implications and possible difficulties of AID must be carefully discussed and considered with the couple. Psychiatric assessment of the couple may be advisable.

I would also insist that a suitable panel of responsible medical men and scientists should be created, comprising *inter alia* a gynaecologist, urologist, psychiatrist and geneticist, for the selection of donors. Naturally most careful attention would have to be paid to secrecy. I realize that such a panel might have its disadvantages, particularly in regard to secrecy and anonymity. Perhaps it would also be wise to insist on a second specialist opinion in every case where AID is contemplated.

That we are dealing here with something that can bring happiness to a number of people is quite certain; but equally there can be no doubt that if this thing is not properly controlled by the law, and by suitably constituted bodies of responsible men and women, it may be charged with risk and danger of the highest degree (particularly if it gets out of hand and is practised by unskilled or unscrupulous people)—danger to the individuals immediately concerned (including the doctor), to their families, to their race, and to humanity in general.

My own feeling about AID is summed up in a poem which I would like to quote. It is called *Die Beiteltjie* (The Little Chisel) and is by N. P. van Wyk Louw,[8] one of the foremost poets in the Afrikaans language. Perhaps it is only fair to say I am sure that AID was far from the poet's mind when he wrote it:

DIE BEITELTJIE

Ek kry 'n klein klein beiteltjie,
ek tik hom en hy klink;
toe slyp ek en ek slyp hom
totdat hy klink en blink.

Ek sit 'n klippie op 'n rots:
— mens moet jou vergewis:
'n beitel moet kan klip breek
as hy 'n beitel is —

ek slaat hom met my beiteltjie
en dié was sterk genoeg:
daar spring die klippie stukkend
so skoon soos langs 'n voeg:

toe, onder my tien vingers bars
die grys rots middeldeur
en langs my voete voel ek
die sagte aarde skeur,

die donker naat loop deur my land
en kloof hom wortel toe —
só moet 'n beitel slaan
wat beitel is, of hoé?

Dan, met twee goue afgronde
val die planeet aan twee
en oor die kranse, kokend,
verdwyn die vlak groen see

en op die dag sien ek die nag
daar anderkant gaan oop
met 'n bars wat van my beitel af
dwarsdeur die sterre loop.

SUMMARY

Artificial insemination with a donor's semen (AID) is discussed from the point of view of a gynaecologist.

The historical aspect of the subject is surveyed, beginning with references to ancient Jewish and Arab writings.

The technique of AID is described, with mention of the medical and legal precautions to be taken.

Reference is made to some of the moral and legal objections to the practice of AID.

In drawing his conclusions the author feels that, all things considered, the practice of AID is undesirable, but that if it is not legally prohibited greater protection should be given to the individuals directly concerned.

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ACUTE PORPHYRIA IN A BANTU MALE

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Porphyria with cutaneous manifestations is by no means rare in Bantu subjects in South Africa and these patients do not seem to be liable to the episodes of abdominal pain and paralysis that are frequently seen in White porphyrics in this country. Acute porphyria without cutaneous lesions is not unknown in the Bantu but is encountered so rarely that reports of cases are justifiable as a reminder that they exist and should be fully investigated, for there are still several unanswered questions about aetiology, progress, and their relationship to other forms of porphyria.

CASE RECORD

The present patient, M.S., an intelligent Chwana male aged 33 years, was admitted to Klerksdorp Hospital on 25 September 1958 for investigation. He had been an underground labourer and had spent the preceding week in the mine sick-bay with a febrile illness. His symptoms were non-specific, with no particular dyspnoea or abdominal pain. Examination was essentially negative, though he appeared to have lost weight. His skin was thin and inelastic but showed no ulcers or scars. The urine was normal to ward tests; there were no faecal pathogens; sputa were negative for *M. tuberculosis*. Chest X-ray revealed a moderate increase in cardiac diameter and miliary nodulation in the lung fields. On a presumptive diagnosis of miliary tuberculosis, streptomycin, rimifon and PAS were started in full dosage on 2 October. The temperature, which had been swinging to 101° F, gradually settled to normal by the 16th.

Then in the course of a few days he developed a striking palsy of the muscles of the pelvic and shoulder girdles. He was unable to elevate his arms at the shoulder against gravity, though elbow and hand movements were of normal power; he could not raise his legs at the hips while in bed, and walked with great difficulty and a waddle. Knee and ankle movements were strong. Tendon reflexes were normal and there was no sensory disturbance. Lumbar puncture revealed nothing apart from a low chloride (109 mEq./litre). Wassermann reactions on blood and spinal fluid were negative. Blood count showed a moderate anaemia (Hb. 10·2 g.%) and a slight leucopenia (4,600 leucocytes per c.mm.).

Skin and muscle biopsies on 23 October were strongly suggestive of a collagen disease, which was then thought to account for the entire picture, and he was discharged to the mine without further treatment. An interesting feature was that the biopsy wound, which was not infected, dehisced on removal of the stitches on the 7th day.

The girdle paralysis abated completely though gradually, but he never looked or felt well and did not return to underground work.

On 20 April 1959 he was seen again with dependent oedema, considerable dyspnoea, and elevated jugular venous pressure. Conjunctival pallor was noted. The urine contained no albumen but was of a darkish colour, which became somewhat more intense on standing. A specimen sent to Johannesburg was found to contain moderate amounts of porphyrin and porphobilinogen, whereupon the patient was transferred to the Non-European Hospital, Johannesburg, on 5 May for further investigation.

He here complained of a 'ball in his stomach' (right upper abdominal quadrant) for the past 7 weeks but there was no associated pain and he had not vomited. The variable facial oedema had sometimes made vision difficult. He had been coughing a good deal and producing sputum for 3 weeks. There was dyspnoea on effort but no chest pain. Physical examination indicated congestive cardiac failure but there were no clinical signs or symptoms attributable to porphyria. He later developed thrombophlebitis in his right leg, and on 16 May pulmonary embolism occurred and anticoagulant therapy was instituted. Though sputum was consistently negative for *M. tuberculosis*, X-ray again showed miliary mottling and anti-tuberculous treatment was resumed.

He developed a queer mental state progressing to dementia, became extremely weak and emaciated, and died on 27 July. Autopsy revealed the presence of generalized tuberculosis.

Stools had been analysed for porphyrins on 12 and 29 May. These contained 68 and 78 μg. of coproporphyrin and 47 and 76 μg. of protoporphyrin respectively per g. dry weight. Small amounts of porphyrin were found on spectroscopic examination in a number of specimens of urine, and aminolaevulic acid (ALA) and porphobilinogen (PBG) assays by the procedure of Mauzerall and Granick[1] were as follows:

		ALA	PBG
		(mg. per litre)	
May	5	6	17
,,	11	6	14
,,	28	18	52
,,	30	12	53
June	2	14	63
,,	8	11	38
,,	13	9	32
,,	19	17	47
Normal		less than 4	less than 1

It was impossible, unfortunately, to continue these examinations, but urine obtained at autopsy contained but a trace of porphyrin and gave a negative Watson-Schwartz test for porphobilinogen. The screen test on a fragment of rectal contents indicated a slight excess of porphyrin. Liver tissue contained 1·7 μg. per g. of ether-soluble porphyrin and 29 μg. per g. of porphyrin that was not soluble in ether.

Family history. The patient referred to his paralytic episode as rheumatism and stated that his father had been similarly affected. On examination the father proved to be a very well preserved Native apparently over 70 years of age. Examination of his central nervous, cardiovascular and respiratory systems revealed no abnormality. The skin of his face and forearms was very dark, in contrast to the medium reddish-brown of protected areas, but no ulceration or scarring were observed and there was no temporal hirsutism. He gave no history of abdominal pain but stated that he had had 'rheumatism' in his legs which was disabling, and that he could not, on this account, do hard work. He was cheerful and loquacious, referring several times to urinary disability but denying ever passing red urine. No porphyrin was detected on spectroscopic examination of a freshly passed specimen. The Watson-Schwartz test showed a slight excess of urobilinogen and a faint pink tinge remained in the aqueous phase. Next morning, however, this specimen contained 2·3 mg. of aminolaevulic acid and less than 1 mg. of porphobilinogen per litre. His wife, mother of the propositus, had died 3 years previously complaining of feeling 'bad in her body'. She had refused to go to hospital. After preparing an evening meal she complained of pain in her chest and died during the night. A sister of the patient lived in the neighbourhood, and the patient also had 2 children, but none of these was available for examination.

DISCUSSION

Salient points in this history are the episode of paralysis, the observation some months later of dark urine the colour of which deepened appreciably on standing, and the finding within the next few weeks of porphyrin together with moderate increases of aminolaevulic acid and porphobilinogen in several specimens of urine. Had these been found at one and the same time acute porphyria could scarcely have been in doubt, and even when spread over half a year they are strongly suggestive of this diagnosis. The low chloride in the spinal fluid at the time of the paralysis also fits into the picture, since there was no clinical evidence of tuberculous meningitis at that time. The tuberculosis, though it was responsible for the fatal termination, seems not to have aggravated the porphyria, for the urine obtained at autopsy did not suggest an exacerbation of the porphyric condition.

Several cases of acute porphyria have been seen in past years in Bantu patients but this is the first to be studied in detail by methods now available. None of them showed evidence of skin eruptions, which suggests that they may fall into a different group from the variegate porphyria in White South Africans,[2] where cutaneous lesions are not uncommon. In this respect the Bantu patients conform to the classical intermittent acute porphyria reported from other parts of the world, notably Sweden. The biochemical findings in the present patient likewise conform in that urinary excretion of aminolaevulic acid and porphobilinogen was still significantly elevated during a clinical remission some months after the paralytic episode.[3] The stool porphyrins, though slightly above normal, were well below the level commonly found in patients with variegate porphyria.

Waldenstrom[4] has established beyond doubt that intermittent acute porphyria in Sweden follows the Mendelian dominant rule of inheritance. There is, thus far, no satisfactory evidence of heredity in the cutaneous form of porphyria which is common in South African Bantu. No indications of porphyria were found in our patient's father and the meagre information available about his mother does not suggest that her death could be attributed to this condition. This aspect of the case remains incomplete, because several immediate relations eluded examination.

Several other cases of acute porphyria in African Natives have been reported in some detail.[5-9] It is hoped that more instances will become available for detailed investigation by methods now at our disposal so that answers may be found to the obvious questions.

SUMMARY

A case of acute porphyria in a Bantu male is presented. The findings differed in several respects from those in White South African patients with variegate porphyria but conformed to the pattern of the intermittent acute form. No evidence of heredity was obtained but not all members of the family were available for study.

We have to thank the Director of the South African Institute for Medical Research for providing facilities for the laboratory studies and Dr. P. Keen, Superintendent of the Non-European Hospital, Johannesburg, for admitting the patient for closer observation.

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TRIAL OF AN ORAL DIURETIC, HYDROCHLOROTHIAZIDE

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Hydrochlorothiazide has been introduced as an oral diuretic agent with a potency considered greater than that of any other oral agent, and has been submitted to clinical trial by various observers.[1-10] In general its efficacy has been confirmed, although there is disagreement concerning the loss of potassium which it induces,[11] and its potency compared with other diuretics. In the present study the effect of a relatively large single oral dose, 250 mg., is compared with that of 2 c.c. of a parenteral mercurial, mersalyl, in the same patients. This oral dose was chosen after preliminary trials with single doses increasing from 50 to 250 mg. had indicated increasing effect until at the higher figure a water diuresis equivalent to that of 2 c.c. of mersalyl was obtained.

Methods

Eleven patients kept at bed rest in hospital were studied. All were suffering from chronic congestive heart failure—due in 1 to essential hypertension, in 3 to constrictive pericarditis, in 3 to rheumatic valvular disease, and in 4 to African cardiomyopathy. All were on digitalis therapy and a low-salt diet (approx. 400 mg. per day) and initially were closely observed after a state of equilibrium in congestive heart failure had been achieved. This observation period lasted for a minimum of 1 week. The blood urea and serum concentrations of sodium, potassium and chloride were determined and the urine examined before the beginning and at the end of the trial. The height of the jugular venous pulse and the degree of oedema and hepatomegaly were assessed daily from the beginning of the period of close observation. From the first day of the trial, daily 24-hour volumes of urine were collected; their content of sodium, potassium and chloride were estimated in 9 of the patients. At the end of the first 24-hour period, 2 c.c. of mersalyl was injected, and at the end of the 4th period 250 mg. of hydrochlorothiazide was given by mouth. The mersalyl was repeated at the end of the 8th period, i.e. 1 week after the first injection, and hydrochlorothiazide was repeated at the end of the 11th period, 1 week after its first administration. This weekly administration of each drug in turn was continued for a varying time (Table I). Results were calculated for mersalyl by obtaining for each patient the ratio of the sums of outputs of water, sodium, potassium and chloride respectively in the 24-hour periods preceding the mersalyl injections to the sums of outputs in the 24-hour period succeeding the injections. Results for hydrochlorothiazide were obtained similarly. In all tests, as described above, the drugs were given alternately. As the trial lasted for a varying number of weeks in different patients, the mean ratios for the whole series were calculated not from the individual patient-ratios, but from all tests considered together.

Results

On this regime the patients showed no change in blood-urea or serum-electrolyte concentrations, the initial values of which were all normal, and in no patient was there any abnormal urinary finding after the trial. In all the patients there was gradual improvement as regards the heart failure. Other patients not in this series with less severe and less chronic heart failure have shown the same picture of rapid recovery when treated with digitalis and hydrochlorothiazide that is seen when parenteral mersalyl is used as the diuretic. No toxic effects were observed.

The results of excretion measurements are set out in Tables I-IV.

Urine volume. From Table I it is apparent that among the different patients there was a wide range of response to mersalyl and to hydrochlorothiazide, one patient, with constrictive pericarditis (case 1) showing a more than 5-fold increase in urine output after both drugs, and one patient (case 9) showing no response to mersalyl at all. It is possible that the slightly lower 24-hour volumes preceding hydrochlorothiazide compared with the volumes preceding mersalyl may have prejudiced the results against hydrochlorothiazide; but the distribution of the individual patients' tests relating volumes before mersalyl to volumes after mersalyl, and similarly for hydrochlorothiazide, showed a complete scatter, so that this factor cannot be considered to be operating. That the giving of mersalyl as the initial diuretic made no difference to the results is shown by the fact that if the first mersalyl result was ignored in calculating the before-after ratios, no significant difference was observed. This can be explained by the relatively refractory heart failure in all these patients, so that their clinical state varied only slowly. The ratios for all tests of urine-volume output are similar for mersalyl and hydrochlorothiazide, 1 : 1·77 and 1 : 1·61.

Sodium and chloride outputs. The saluretic effects of the drugs is shown by their high before-after administration ratios, appreciably higher than their urine-volume ratios and of the same order for sodium as for chloride. Both with mersalyl and with hydrochlorothiazide the difference between the outputs of these two substances is not statistically significant ($p > 0·2$). Moyer *et al.*[7] on the other hand considered on their figures that the primary effect seemed to be on chloride excretion, there being nearly always a greater increase in chloride than in sodium excretion. The same variation in response to the drugs is seen with sodium and chloride as it is with water; patient E.D. (case 1) produced a before-after ratio with hydrochlorothiazide of 1 : 52·6 for chloride, and 1 : 36·9 for sodium. The equivalent figures for patient N.N. (case 3), who showed the least response, are 1 : 1·42 and 1 : 1·39.

Potassium. The excretion of potassium is considerably less promoted by both drugs than the excretion of sodium and chloride. Although at this dose there is a potassium excretion of 1·59 times the control level after hydrochlorothiazide, this before-after ratio is not significantly greater than the ratio 1 : 1·14 for mersalyl ($p = 0·1$).

TABLE I. URINE VOLUME SUMS, IN C.C.

Patient	No. of Tests		Periods		Periods		Before/After Ratios	
	Mers.	Hyd.	Before Mers.	After Mers.	Before Hyd.	After Hyd.	Mers. 1:	Hyd. 1:
1. E.D. ..	4	4	1,790	9,930	1,160	8,965	5·55	7·73
2. M.C. ..	2	2	1,710	3,570	1,620	4,590	2·09	2·83
3. N.N. ..	3	2	4,510	6,230	2,200	2,680	1·38	1·22
4. M.N. ..	4	3	5,010	9,540	3,900	6,830	1·90	1·75
5. M.Ng. ..	5	5	7,500	13,400	6,180	8,830	1·79	1·43
6. J.X. ..	4	3	3,360	7,300	3,480	3,500	2·17	1·01
7. B.S. ..	10	9	14,640	23,810	11,600	17,410	1·63	1·50
8. J.M. ..	6	5	7,510	15,630	7,170	11,220	2·08	1·56
9. S.H. ..	3	3	5,760	5,700	4,320	6,180	0·99	1·43
10. J.Mz. ..	4	3	7,560	10,620	5,400	6,600	1·40	1·22
11. A.N. ..	4	5	4,460	7,430	5,560	8,070	1·67	1·45
Totals ..	49	44	63,810	113,160	52,590	84,875		
Ratio:			1: 1·77		1: 1·61			

TABLE II. SODIUM OUTPUT SUMS, IN MILLI-EQUIVALENTS

Patient	No. of Tests		Periods		Periods		Before/After Ratios	
	Mers.	Hyd.	Before Mers.	After Mers.	Before Hyd.	After Hyd.	Mers. 1:	Hyd. 1:
1. E.D. ..	4	4	126	1,006	21	775	8·00	36·90
2. M.C. ..	2	2	51	246	28	424	4·82	15·14
3. N.N. ..	3	2	364	619	189	263	1·70	1·39
4. M.N. ..	2	1	106	465	115	209	4·39	1·82
5. M.Ng. ..	5	5	470	1,367	246	647	2·90	2·63
6. J.X. ..	4	3	255	756	138	313	2·97	2·27
7. B.S. ..	9	9	605	1,823	271	949	3·01	3·50
8. J.M. ..	4	4	410	1,054	172	610	2·57	3·55
11. A.N. ..	4	5	155	553	146	383	3·57	2·62
Totals ..	37	35	2,542	7,889	1,326	4,573		
Ratio:			1: 3·1		1: 3·45			

TABLE III. POTASSIUM OUTPUT SUMS, IN MILLI-EQUIVALENTS

Patient	No. of Tests		Periods		Periods		Before/After Ratios	
	Mers.	Hyd.	Before Mers.	After Mers.	Before Hyd.	After Hyd.	Mers. 1:	Hyd. 1:
1. E.D. ..	4	4	117	182	33	295	1·56	8·93
2. M.C. ..	2	2	89	122	78	196	1·38	2·51
3. N.N. ..	3	2	148	119	92	74	0·80	0·80
4. M.N. ..	2	1	109	117	148	63	1·07	0·43
5. M.Ng. ..	5	5	218	250	181	236	1·15	1·30
6. J.X. ..	4	3	173	155	130	165	0·89	1·27
7. B.S. ..	10	9	453	616	325	496	1·36	1·53
8. J.M. ..	4	4	177	176	162	305	1·00	1·88
11. A.N. ..	4	5	198	174	177	279	0·88	1·57
Totals ..	38	35	1,682	1,911	1,325	2,109		
Ratio:			1: 1·14		1: 1·59			

TABLE IV. CHLORIDE OUTPUT SUMS, IN MILLI-EQUIVALENTS

Patient	No. of Tests		Periods		Periods		Before/After Ratios	
	Mers.	Hyd.	Before Mers.	After Mers.	Before Hyd.	After Hyd.	Mers. 1:	Hyd. 1:
1. E.D. ..	3	4	58	932	19	1,000	16·07	52·63
2. M.C. ..	2	2	87	378	31	587	4·34	18·93
3. N.N. ..	3	2	420	645	186	264	1·54	1·42
4. M.N. ..	2	1	138	363	156	239	2·63	1·53
5. M.Ng. ..	5	5	606	1,314	268	812	2·17	3·03
6. J.X. ..	3	2	279	571	176	367	2·04	2·07
7. B.S. ..	10	9	586	1,579	347	1,136	2·69	3·28
8. J.M. ..	4	4	324	1,109	240	717	3·42	2·99
11. A.N. ..	4	5	224	639	118	427	2·85	3·53
Totals ..	36	34	2,722	7,530	1,541	5,549		
Ratio			1: 2·77		1: 3·60			

Discussion

The results show that this single oral dose, 250 mg., of hydrochlorothiazide produces a diuresis of water, sodium, potassium and chloride similar to that of 2 c.c. of parenteral mersalyl, and that the potassium excretion is minor. The mean increase of potassium excreted over control values was 22 mEq. in the 24 hours following administration. This figure would certainly be greater in more responsive patients, as is indicated by the dose-response curve of Moyer *et al.*, where the figure is about 65 mEq. The dose of hydrochlorothiazide used in this study is higher than that used in trials by others[4-6] but is comparable to the 200 mg. dose used by Moyer *et al.* Since it appears to lie at the peak of the dose-response curve of Moyer *et al.*, it is probably optimal for single dose administration. The amounts used by others have been designed for daily maintenance therapy and are therefore not comparable with a dose designed for single administration. Various authors[1,3,5] have reported that maintenance can be achieved with between 25 and 100 mg. a day.

SUMMARY

A single oral dose of 250 mg. of hydrochlorothiazide was tested alternately with a single parenteral dose of 2 c.c. of mersalyl in a series of patients with chronic heart failure.

The two drugs produced similar diureses of water, sodium, potassium and chloride. Those of sodium and chloride were marked, that of potassium, minor. Toxic effects were not observed.

It is concluded that a single oral dose of 250 mg. of hydrochlorothiazide forms a substitute for a single parenteral dose of 2 c.c. of mersalyl.

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INAUGURAL PRESIDENTIAL ADDRESS*

F. N. GILLWALD, *President, O.F.S. Goldfields Branch (M.A.S.A.)*

On behalf of the Officers of this Branch and myself I thank you all for the confidence you have displayed in us by electing us as the first Branch Council. We will endeavour to deserve the trust you have placed in us and to conduct the affairs of this Branch as efficiently as possible.

I should like to welcome our many visitors to this meeting, and to thank you one and all for the time you have given up to be with us. Some of you have travelled vast distances to be with us at this first Annual General Meeting and we hope that when you leave you will feel that it has all been worth-while. Our invitations to you were based, I can assure you, on the most selfish motives. Not only do we want the pleasure of your company and your moral support, but we look to you, particularly the more senior and experienced visitors, to give us what advice you can to help this new Branch to build a sturdy foundation for the future. It is one of the disadvantages of this vast country of ours that our profession is so widely scattered that few of us have the pleasure of meeting the leaders of the Medical Association. We all know by name and reputation who the President of the Medical Association is, and who the Chairman of the Federal Council is and who the President of the Orange Free State Branch is, but until today most of us will not have met you. The getting together of the members of the Association from far and wide is probably the most important function that this meeting will serve and only good can come out of the contacts, the exchanges of ideas and appreciation of one another that must follow. It is an invidious task to name only a few of the guests assembled here this afternoon, as all our guests are equally welcome, but I should like to introduce to you: Dr. P. F. H. Wagner, of East London, the President of the Medical Association of South Africa; Dr. J. H. Struthers, of Pretoria, Chairman of Federal Council; Dr. G. F. C. Troskie, of Kroonstad, President of the Orange Free State and Basutoland Branch; and Dr. P. D. Combrink, Assistant Secretary of the Medical Association.

Having attained Branch status and before we allow the heady atmosphere of this high altitude to bemuse our thinking, let us pause and look round from the new elevation at the perspectives about us.

Problems and Obligations

We now form a separate small Branch in the federal type of government into which the Medical Association has organized itself. As such, we have, provided we remain within the framework of the principles laid down by the Association, a more direct say in the handling of our internal affairs than we had as a Division. We also now have direct representation on the Federal Council. This greater freedom brings with it greater responsibilities. Before making decisions in the future we shall have to bear in mind the fact that the consequences may extend beyond the borders of our area and affect neighbouring Branches, just as decisions of neighbouring Branches may, in matter of common interest, affect us. In these matters of common interest a satisfactory solution can only be reached by joint consultation, negotiation, and compromise so that the Branches concerned can present to the Association and to the outside world a workable scheme of action.

It has, perhaps, been one of the causes of friction within the Association, that large and powerful Branches, seeing a problem only through their own eyes, have been able to sway the Association into accepting their solution to the detriment of other Branches with the same problem, but under somewhat different circumstances. I therefore welcome the formation of new and smaller Branches within the Association such as we are forming today. This may eventually lead to the acceptance of the principle of differential solutions to problems which affect several Branches, so that each Branch may, with the understanding and cooperation of its neighbours, reach the most advantageous solution of its problem within the general terms of reference as laid down by the higher Councils of the Association.

Great pressure is brought to bear on the Medical Association by the Government and by financial and other lay groups, and the utmost in cooperation between the Branches themselves and between the Branches and the Medical Association will be needed so that a firm front may be offered to these forces. It has been encouraging to note that some of the anomalies pertaining to benefit societies are being removed at the moment and a far firmer and consistent attitude to benefit societies than that which existed a few years ago can be sensed. The medical aid society conception is sound. It allows a large number of people in the lower middle class, financially speaking, to obtain the standard medical service they might not be able to afford individually and, at the same time, their medical attendant gets an adequate remuneration.

The various medical insurance schemes are sound in concept but the methods adopted by some of the companies recently, (i) to obtain tariffs to which they are not entitled, (ii) to undermine with insidious propaganda the Medical Association, and (iii) to reduce benefits to their contributors and to suggest to them that doctors who do not reduce their fees in proportion to the lessened benefits are not quite playing the game, can only be deplored. This type of action can only be countered by unanimous determination by the profession to uphold the principles laid down by the Association. The next phase in the

* Address delivered at the first Annual General Meeting of the O.F.S. Goldfields Branch (M.A.S.A.), Welkom, 13 February 1960.

development of this struggle must inevitably be negotiation between the Association and the financial interests concerned, and it is here that the Association may be severely tested as never before. There is no easy answer to the problems but, whatever solution is reached, the Association must ensure that the profession emerges in control of its own destiny, free of lay bureaucracy and united in strength.

Having cast a glance over some of the problems of the wider world, let us examine the lie of the land closer to home. Before raising our voice in the higher Councils of the Medical Association let us put our own house in order. Let us use this occasion to reaffirm the promises and resolutions we have made in the past. We have much in our favour. I doubt whether any other Branch in the country can boast of 100% membership of all the doctors in private practice, within its area. We can present a united front to the rest of the world.

The Principle of Service

In our personal attitude let us adopt the highest ethical standards towards our colleagues and our patients. Let us endeavour to be tolerant, understanding and kindly when faced with the many aggravations encountered in our daily rounds. Let us act with dignity in both our personal and public lives so that the honoured title 'doctor' will symbolize to those around us in this area what we ourselves would like it to do. Let avarice be tempered by consideration of others, greed by fairness, and self-interest by generosity. Let our main reward be satisfaction in the service we have rendered and not in the cheque that follows. Conscientious endeavour to maintain these high standards will enhance the prestige our profession has gained over the years and this new Branch will flourish in the moral and spiritual strength of its members.

Finally, I should like to place on record our appreciation of our neighbours and colleagues, the members of the Orange Free State and Basutoland Branch. From the beginning we have given them continuous headaches, yet we always met with courtesy from them and we were given the privilege of conducting our own affairs as they related to the special problems affecting this portion of their territory. Being in the same Province we share many common interests and we shall always have to work hand in hand. We salute you as our mother Branch and trust that you will go from strength to strength.

BRITISH MEDICAL ASSOCIATION

C. H. MILBURN PRIZE (1960)

This Prize, for an essay or study on a subject of *forensic medicine*, is offered for the first time in 1960, and is of £100 in value. Any registered medical practitioner is eligible to compete.

Entries must consist of original and unpublished material, and preliminary notice of entry is required. Forms and further particulars may be obtained from The Secretary, BMA House, Tavistock Square, London, W.C.1.

Closing date for entries: 31 October 1960.

BRITISH MEDICAL ASSOCIATION IN AUSTRALIA

HENRY SIMPSON NEWLAND PRIZE IN SURGERY

The Henry Simpson Newland Prize in Surgery, established to commemorate the services of Sir Henry Newland to the medical profession, is open for competition. The conditions are:

1. The Prize shall be awarded every 3 years to the writer of the essay adjudged to be the best on a surgical subject.
2. The Prize will consist of a money award of one hundred pounds (£100), together with a medal.
3. The next award will be made in 1962, the subject of the essay being: *The modern management of inflammatory and neoplastic diseases of the left colon and rectum.*
4. The dissertation should be based on personal observation and experience.
5. The essay must be typewritten or printed in English. It must be distinguished by a motto and accompanied by a sealed envelope containing the name and address of the author and having on its outside the corresponding motto. It must not exceed 50,000 words.
6. Essays must be delivered to the General Secretary, Federal Council of the British Medical Association in Australia, 135 Macquarie Street, Sydney, not later than 15 January 1962.
7. The competition is open to any graduate of any medical school within the British Commonwealth.
8. The Committee administering the Henry Simpson Newland Prize Fund reserves the right to withhold the Prize and its decision in regard to any award shall be final.
9. The Prize Essay shall be submitted forthwith to the Editor, *The Medical Journal of Australia.*

RAAD OP ATOOMKRAG : ATOMIC ENERGY BOARD

GEBRUIK VAN RADIUM EN SY ONTBINDINGSPRODUKTE

Die Raad op Atoomkrag het gevra dat die aandag van die mediese professie gevestig moet word op die feit dat kragtens die wysigings wat in 1958 in die Atoomkragwet aangebring is, niemand meer radium of sy ontbindingsprodukte mag gebruik sonder die skriftelike magtiging van die Raad nie.

Dit het onder die aandag van die Raad gekom dat daar verskeie mediese praktisyns is wat radiumbronne besit en dit gebruik sonder die magtiging van die Raad. Alle persone wat radium in hulle besit het moet onverwyld aansoek doen vir magtiging om dit te besit en te gebruik.

Op die oomblik word daar net magtigings gegee aan radioloë wat op die Spesialiteitsregister van die Suid-Afrikaanse Geneeskundige en Tandheelkundige Raad is om radium en sy ontbindingsprodukte te gebruik.

USE OF RADIUM AND ITS BREAKDOWN PRODUCTS

The Atomic Energy Board has requested that the attention of the medical profession be drawn to the fact that under the terms of the Atomic Energy Act of 1958 no-one may use radium or its breakdown products without the written permission of the Board.

It has come to the notice of the Board that certain medical practitioners have in their possession, and are using, radium sources without the permission of the Board. All persons who have radium in their possession must apply immediately for permission to possess and use it.

At the moment permission has only been given to radiologists on the Specialist Register of the South African Medical and Dental Council to use radium and its breakdown products.

BOEKE ONTVANG : BOOKS RECEIVED

Statistical Methods in Biology. By N. T. J. Bailey, M.A., D.S.C. Pp. ix+200. Figures. 25s. net. London: The English Universities Press Ltd. 1959.

British National Formulary 1957. 2nd Amendment 1959. Pp. 4. 3d. + 2d. postage (orders should be accompanied by the remittance). London: The British Medical Association and The Pharmaceutical Press. 1959.

Miscellaneous Notes (Third Series). By F. Parkes Weber, M.D., F.R.C.P., F.S.A. Pp. 8. 2s. 6d. London: H. K. Lewis & Co. Ltd. 1959.

Modern Surgery for Nurses. 4th edition. Edited by F. Wilson Harlow, M.B., B.S. (Durham), F.R.C.S. (Eng.). Pp. xxiv+883. 419 figures. 30s. net. London: William Heinemann Medical Books Ltd. 1959.

AMPTELIKE AANKONDIGING : OFFICIAL ANNOUNCEMENT

GOEDGEKEURDE MEDIESE HULPVERENIGINGS

Hieronder verskyn die lys van goedgekeurde mediese hulpverenigings soos op 1 April 1960. Lede behoort hierdie lys vir naslaandoeleindes byderhand te hou.

L. M. Marchand
Medesekretaris

Plaza-gebou 28
Pretoria
24 Maart 1960

1. A.A. Mutual Medical Aid Society, P.O. Box 9595, Johannesburg.
2. Abercom Group Sick Benefit Society, P.O. Box 494, Port Elizabeth.
3. African Cables Medical Benefit Fund, P.O. Box 172, Vereeniging.
4. African Explosives Medical Aid Society, P.O. Box 1122, Johannesburg.
5. African Homes Trust Sick Fund, P.O. Box 93, Cape Town.
6. African Oxygen Limited Medical Aid Society, P.O. Box 5404, Johannesburg.
7. Afrikaanse Pers Beperk se Siekefonds, Posbus 845, Johannesburg.
8. Alex, Aitken & Carter Medical Benefit Society, P.O. Box 2636, Johannesburg.
9. Algoa Medical Aid Society, P.O. Box 369, Port Elizabeth.
10. Argus Medical Benefit Society (Cape Argus Branch), P.O. Box 56, Cape Town.
11. Argus Medical Benefit Society (Daily News Branch), P.O. Box 1491, Durban.
12. Argus Medical Benefit Society (Star Branch), P.O. Box 1014, Johannesburg.
13. Associated Employers' Medical Aid Society, P.O. Box 7462, Johannesburg.
14. A.T.I. Medical Aid Society, P.O. Box 5057, Boksburg North.
15. Babcock and Wilcox Medical Aid Fund, P.O. Box 545, Vereeniging.
16. Bakers Ltd. European Employees' Sick Benefit Fund, P.O. Box 692, Durban.
17. Bloemfontein Municipal Employees' Medical Aid Society, P.O. Box 288, Bloemfontein.
18. Boart and Hard Metal Products Medical Aid Society, P.O. Box 9325, Johannesburg.
19. Boksburg Municipal Employees' Medical Aid Fund, P.O. Box 215, Boksburg.
20. Broderick Medical Aid Society, P.O. Box 186, Vereeniging.
21. Building Societies Joint Medical Aid Fund, P.O. Box 5728, Johannesburg.
22. S. Butcher & Sons Ltd. Medical Aid Society, P.O. Box 1004, Durban.
23. Cape Portland Medical Aid Society, P.O. Box 1067, Cape Town.
24. Cape Times Medical Aid Society, P.O. Box 11, Cape Town.
25. Cape Town Municipal Employees' Association Medical Aid Society, P.O. Box 1939, Cape Town.
26. Central News Agency Ltd. Medical Benefit Society, P.O. Box 1033, Johannesburg (excluding Cape Town and suburbs, Durban municipal area, Johannesburg and Witwatersrand, and Port Elizabeth and Pretoria municipal areas).
27. Chamber of Mines Medical Aid Society, P.O. Box 809, Johannesburg.
28. Civil Service Medical Benefit Association, P.O. Box 176, Pretoria.
29. Consolidated Glassworks Limited Medical Aid and Sick Benefit Society, P.O. Box 562, Germiston.
30. Corner House Insurance Fund, P.O. Box 1056, Johannesburg.
31. Coronation Medical Aid Society, P.O. Box 1517, Durban.
32. Crookes Bros. Ltd. Medical Benefit Fund, 301 Smith Street, Durban.
33. D.F.A. Medical Benefit Society, P.O. Box 610, Kimberley.
34. Dorman Long (P.E.) Medical Aid Society, P.O. Box 9010, Port Elizabeth.
35. Eastern Province Cement Co. Ltd. Medical Aid Society, P.O. Box 2016, Port Elizabeth.
36. E.P. Newspapers Medical Aid Society, P.O. Box 1117, Port Elizabeth.
37. Egnep Medical Aid Society, P.O. Penge, Transvaal.

APPROVED MEDICAL AID SOCIETIES

The following is the list of approved medical aid societies as at 1 April 1960. Members should keep this list for reference.

L. M. Marchand
Associate Secretary

28 Plaza Building
Pretoria
24 March 1960

38. Escom Cape Western Undertaking Medical Aid Society, P.O. Box 117, Cape Town.
39. Escom (N.C.U.) Medical Benefit Society, P.O. Box 30, Colenso, Natal.
40. Escom (N.S.U.) Medical Aid Society, P.O. Box 2408, Durban.
41. Everite Medical Aid Society, P.O. Kliprivier, Transvaal.
42. Federated Employers' Medical Aid Society, P.O. Box 666, Johannesburg.
43. Federation of Master Printers of S.A. Medical Aid Society, P.O. Box 4465, Johannesburg.
44. Friend Medical Aid Fund, P.O. Box 245, Bloemfontein.
45. General Mining (Associated Companies) Medical Aid Society, P.O. Box 1007, Johannesburg.
46. General Motors Medical Aid Scheme, P.O. Box 1137, Port Elizabeth.
47. Germiston Industries Medical Aid Society, 113 Pylon House, Human Street, Germiston.
48. Gledhow-Chaka's Kraal Sugar Co. Ltd. Medical Benefits Fund, P.O. Box 55, Stanger, Natal.
49. Goldby, Panchaud and Webber Medical Benefit Fund, P.O. Box 1172, Johannesburg.
50. Greatermans Medical Aid Society, P.O. Box 5460, Johannesburg.
51. Hubert Davies Johannesburg Staff Medical Aid Society, P.O. Box 1386, Johannesburg.
52. Sir J. L. Hulett & Sons Ltd. Medical Benefit Fund, P.O. Box 248, Durban.
53. Hunt, Leuchars & Hepburn Ltd. (Transvaal Staff) Medical Aid Society, P.O. Box 47, Johannesburg.
54. I.C.T. Medical Aid Society, P.O. Box 7018, Johannesburg.
55. Iscor Medical Benefit Fund, P.O. Box 450, Pretoria.
56. I.W.S. Medical Aid Society, P.O. Box 6946, Johannesburg.
57. J. W. Jagger & Co. Ltd. Medical Aid Society, P.O. Box 726, Cape Town.
58. Johannesburg Board of Executors' Medical Aid Society, P.O. Box 271, Johannesburg.
59. Klerksdorp Munisipale Werknemers Siektefonds, Posbus 99, Klerksdorp.
60. K. & L. Timbers Ltd. Staff Medical Aid Fund, P.O. Box 9, Elandsfontein, Transvaal.
61. Koegas Medical Aid Society, P.O. Koegasbridge, C.P.
62. Krantzberg Mines Medical Aid Society, P.O. Box 18, Omaruru, S.W.A.
63. Kroonstad Munisipale Mediese Hulpvereniging, Posbus 302, Kroonstad.
64. Legal and General Medical Aid Society, P.O. Box 4870, Johannesburg.
65. Mail, Times & Express Medical Aid Society, P.O. Box 1138, Johannesburg.
66. Marley Floor Tile Medical Aid Society, P.O. Box 67, Nigel.
67. Masonite Medical Aid Society, P.O. Box 57, Estcourt, Natal.
68. Max Engineering Medical Aid Scheme, P.O. Box 174, Vereeniging.
69. Metal Box Company of S.A. Ltd. Medical Aid Society, P.O. Box 7752, Johannesburg.
70. Municipal Employees' Medical Aid Society (Durban), P.O. Box 625, Durban.
71. Natal Building Society Medical Aid Fund, P.O. Box 947, Durban.
72. Natal Coal Owners' (Durban Staff) Medical Aid Society, P.O. Box 281, Durban.
73. Natal Estates Sick Fund Benefit Society, P.O. Mount Edgecombe, Natal.
74. Natal Industries Medical Aid Society, P.O. Box 1300, Durban.
75. N.T.E. Staff Medical Aid Fund, P.O. Box 39, Pietermaritzburg.

76. National Industrial Credit Corporation Medical Aid Society, P.O. Box 8296, Johannesburg.
77. National Portland Medical Aid Society, P.O. Box 21, Claremont, C.P.
78. National Trading Medical Aid Society, P.O. Box 2762, Johannesburg.
79. New Consolidated Gold Fields Employees' Medical Aid Fund, P.O. Box 1167, Johannesburg.
80. Northern Assurance Co. Ltd. Medical Aid Society, P.O. Box 8615, Johannesburg.
81. Northern Medical Aid Society, P.O. Box 3437, Johannesburg.
82. Northern Rhodesia European Civil Servants, Medical Aid Society, P.O. Box R.W. 13, Ridgeway, N.R.
83. Norwich Union Life Insurance Staff Medical Aid Society, P.O. Box 1226, Cape Town.
84. Ore & Metal Medical Aid Society, P.O. Box 3548, Johannesburg.
85. Pietermaritzburg Chamber of Industries Medical Aid Society, P.O. Box 365, Pietermaritzburg.
86. Pilkington Group European Medical Aid Society, P.O. Box 111, Springs.
87. Polliack Group Medical Aid Society, P.O. Box 3008, Johannesburg.
88. Pongola Sugar Milling Co. Ltd. Medical Benefit Fund. P.O. Box 194, Durban.
89. Post Office Medical Aid Society, P.O. Box 303, Germiston.
90. Pretoria Municipal Employees' Sick Fund, P.O. Box 408, Pretoria.
91. Pretoria News Medical Benefit Society, P.O. Box 439, Pretoria.
92. Pretoria Portland Cement Co. Ltd. No. 1 Works (Hercules), Medical Aid Society, P.O. Box 405, Pretoria.
93. Pretoria Portland Cement Co. Ltd. No. 2 Works Medical Benefit Society, P.O. Box 7, Slurry, Western Transvaal.
94. Pretoria Portland Cement Co. Ltd. No. 3 Works (Jupiter) Medical Aid Society, P.O. Box 73, Cleveland, Transvaal.
95. Pretoria Portland Cement Co. Ltd. No. 4 Works Medical Aid Society, P.O. Box 26, Orkney, district Klerksdorp.
96. Printing Industry Medical Aid Society, P.O. Box 1993, Pretoria.
97. Prudential Medical Aid Scheme, P.O. Box 1097, Johannesburg.
98. Rand Water Board Sick Fund, P.O. Box 1127, Johannesburg.
99. Randles Bros. & Hudson Ltd (Durban) Sick Benefit Fund, P.O. Box 1046, Durban.
100. Randles Bros. & Hudson Ltd. (Johannesburg) Employees' Sick Benefit Fund, P.O. Box 2678, Johannesburg.
101. 'Rennie' and 'The Consolidated' Employees' Medical Aid Fund, P.O. Box 1006, Durban.
102. Reynolds Bros. Ltd. Medical Benefits Fund, 301 Smith Street, Durban.
103. E. S. & A. Robinson (Pty.), Ltd. Medical Aid Society, P.O. Box 293, Germiston.
104. Royal-Globe Medical Aid Fund, P.O. Box 83, Cape Town.
105. Safim Medical Aid Society, P.O. Box 233, Vereeniging.
106. Safmarine Medical Aid Society, P.O. Box 2171, Cape Town.
107. Safnit Mills Medical Aid Fund, P.O. Box 11, Jeppestown, Johannesburg.
108. Santam-Sanlam Siektefonds (alle takke), Posbus 1, Sanlamhof, K.P.
109. Shell Medical Aid Society (S.A.), P.O. Box 2231, Cape Town.
110. S.A. Breweries Medical Aid Society, P.O. Box 1099, Johannesburg.
111. S.A.K.A.V. Sick Benefit Fund, P.O. Box 33, Paarl.
112. S.A. Mutual Fire & General Insurance Co. Ltd. Staff Medical Aid Fund, P.O. Box 516, Johannesburg.
113. S.A. Mutual Life Assurance Society Staff Medical Aid Fund, P.O. Box 66, Cape Town.
114. S.A. Press Association Medical Aid Society, P.O. Box 7766, Johannesburg.
115. S.A. Sugar Association Medical Benefits Fund, P.O. Box 2160, Durban.
116. S.A. Teachers' Association Medical Aid Society, 12 Bellevue Road, Sea Point, C.P.
117. S.A. Torbanite (Boksburg) Medical Aid Society, P.O. Box 5083, Boksburg North.
118. South Atlantic Corporation Medical Aid Society, P.O. Box 1628, Cape Town.
119. Southern Medical Aid Society, P.O. Box 42, Cape Town.
120. Standard Brass Medical Aid Society, P.O. Box 229, Benoni.
121. Steeldale and Union Joinery Medical Aid Society, P.O. Box 1210, Johannesburg.
122. Sun Insurance Office Ltd. Staff Medical Aid Fund, P.O. Box 429, Johannesburg.
123. Sydmore Sick Benefit Society, P.O. Box 8851, Johannesburg.
124. Syfret's Medical Aid Society, 24 Wale Street, Cape Town.
125. Traduna Medical Aid Fund, P.O. Box 8791, Johannesburg.
126. Transvaal Corundum Associated Asbestos Medical Aid Society, P.O. Box 72, Pietersburg, Transvaal.
127. Transvaal Society of Accountants Medical Aid Fund, P.O. Box 2995, Johannesburg.
128. U.L.A. Medical Aid Society, P.O. Box 4589, Johannesburg.
129. Umzimkulu Sugar Co. Ltd. Medical Aid Fund, P.O. Box 43, Durban.
130. United Banks' Medical Aid Society, P.O. Box 1242, Cape Town.
131. United Building Society Medical Aid Fund, P.O. Box 7735, Johannesburg.
132. University of the Witwatersrand (Johannesburg) Staff Medical Aid Fund, Milner Park, Johannesburg.
133. Village Board of Management of Welkom Medical Aid Society, P.O. Box 708, Welkom, O.F.S.
134. Wright, Boag & Head, Wrightson Sick Benefit Fund, P.O. Box 183, Benoni.
135. Yorkshire Medical Aid Society, P.O. Box 2755, Johannesburg.

MEDIESE BYSTANDSVERENIGINGS WAT VRY KEUSE VAN DOKTER ALLEEN VIR SPESIALISTEDIENSTE TOELAAT
MEDICAL BENEFIT SOCIETIES WHICH ALLOW FREE CHOICE OF DOCTOR FOR SPECIALIST SERVICES ONLY

1. Begbie Medical Benefit Fund, P.O. Box 192, Middelburg, Transvaal.
2. Brakpan Power Station Sick Benefit Society, P.O. Box 1, Brakpan.
3. Breyten Coalfields Benefit Society, P.O. Box 6, Estantia, Transvaal.
4. Broken Hill Mine Employees' Medical Specialist Fund, P.O. Box 45, Broken Hill.
5. De Beers Consolidated Mines Limited Benefit Society, P.O. Box 616, Kimberley.
6. Durban Roodepoort Deep Ltd. Benefit Society, P.O. Box 193, Roodepoort.
7. Jagersfontein Mine Benefit Society, P.O. Box 2, Jagersfontein, O.F.S.
8. Krugersdorp Municipal Employees' Medical Benefit Society, P.O. Box 101, Krugersdorp.
9. Northern Rhodesia Mine Employees' Medical Specialist Fund, P.O. Box 134, Kitwe, N.R.
10. Public Utility Transport Corporation Sick Fund, P.O. Box 9571, Johannesburg.
11. Randfontein Estates Employees' Sick Benefit Society, P.O. Box 37, Randfontein.
12. Roodepoort-Maraisburg Municipal Employees' Sick Benefit Society, P.O. Box 217, Roodepoort.
13. Roodepoort-Maraisburg Non-Scheduled Mines, and Industries' Benefit Society, P.O. Box 225, Roodepoort.
14. Rosherville-Maraisburg Benefit Society, P.O. Box 99, Cleveland, Johannesburg.
15. Sasol Medical Benefit Society, P.O. Box 80, Sasolburg.
16. Simmer Pan Medical Benefit Society, P.O. Box 103, Germiston.
17. Springs Mines Benefit Society, P.O. Box 54, Springs.
18. Tongaat Sugar Company Medical Benefit Scheme, P.O. Box 5, Maidstone, Natal.
19. Transvaal Jewellers' & Goldsmiths' Sick Benefit Fund, P.O. Box 8530, Johannesburg.
20. Tweefontein Colliery Employees' Benefit Society, Tweefontein Colliery, P.O. Coalville, Transvaal.
21. Western Province Building & Allied Trades Sick Fund, P.O. Box 2013, Cape Town.
22. Witbank Coalfields Benefit Society, P.O. Box 26, Witbank.
23. Witbank Power Station Medical Benefit Society, P.O. Box 197, Witbank.

IN DIE VERBYGAAN : PASSING EVENTS

Dr. Morris J. Cohen, neurologist and psychiatrist, has resumed practice at 40 Musgrave Centre, Musgrave Road, Durban. Telephones: Rooms 45236, residence 888639.

Dr. Morris J. Cohen, neuroloog en psigiater, het sy praktyk hervat te Musgrave Sentrum 40, Musgraveweg, Durban. Telefone: Spreekkamer 45236, woning 888639.

* * *

Dr. Harry Z. Gelman, B.Sc., M.B., B.Ch. (Rand), D.O. (R.C.P., Lond., R.C.S., Eng.), D.O.M.S. (R.C.P. and S.I.), who has recently returned from overseas, has joined the practice of Dr. Gordon Handelsman as an ophthalmologist at 72 - 4 Pasteur Chambers, Jeppe Street, Johannesburg.

Dr. Harry Z. Gelman, B.Sc., M.B., B.Ch. (Rand), D.O. (R.C.P., Lond., R.C.S., Eng.), D.O.M.S. (R.C.P. en S.I.), het onlangs van oorsee teruggekeer en praktiseer nou saam met dr. Gordon Handelsman as 'n ophthalmoloog te Pasteur Chambers 72 - 4, Jeppestraat, Johannesburg.

* * *

University of Cape Town and Association of Surgeons of South Africa (M.A.S.A.) Joint Lectures. The next lecture in this series will be held on Wednesday 20 April at 5.30 p.m. in the E-floor Lecture Theatre, Groote Schuur Hospital, Observatory, Cape. Dr. R. de Villiers will speak on 'The aortic valve with special reference to the surgical correction of aortic insufficiency'. All members of the Medical Association are welcome.

* * *

South African Institute for Medical Research, Johannesburg, Staff Scientific Meeting. The next meeting will be held on Monday 25 April at 5.10 p.m. in the Institute Lecture Theatre. Dr. I. Bersohn will speak on 'The possible interrelationship between urinary oestrogens, diet and coronary artery disease'.

* * *

College of General Practitioner, Northern Transvaal Faculty. A very well attended dinner was held in Pretoria on 19 February to decide whether or not a Faculty of the College of General Practitioners should be formed in the Northern Transvaal. Members were addressed by Dr. J. H. Struthers and by Dr. Klein, who outlined the reasons for the formation of a Faculty. After lively discussion on the matter it was unanimously agreed that a Faculty be formed in the Northern Transvaal Branch of the Medical Association. Anyone interested in becoming a member should contact Dr. T. P. Venning, of Pretoria, the Hon. Secretary.

* * *

Universiteit van Pretoria, Fakulteit Geneeskunde. Die derde Interdepartementele Bespreking vir 1960 sal Saterdagoggend 23 April om 8.30 vm. in die Onderste Lesingsaal, Kliniese Gebou, plaasvind. Die onderwerp van die bespreking is ‚Fetale anoksie, asphyxia neonatorum en resussitasie van die pasgeborene'. Die Voorsitter is prof. F. G. Geldenhuys. Alle medici wat belangstel in hierdie besprekings is welkom.

* * *

Southern Transvaal Branch (M.A.S.A.). Prof. I. Boerema, Professor of Surgery at the University of Amsterdam, The Netherlands, will deliver a lecture on 'Hiatus hernia' in the Harveian Lecture Theatre, Medical School, University of the Witwatersrand, Johannesburg, on Wednesday 27 April at 8.15 p.m.

* * *

College of General Practitioners, Witwatersrand Faculty. Members and guests are invited to attend a lecture on 26 April at the S.A. Blood Transfusion House, Klein Street, Hospital Hill, Johannesburg, at 8 p.m. when Prof. D. J. du Plessis, Professor of Surgery at the University of Witwatersrand, will lecture on 'Cholecystitis'.

* * *

Association of Physicians of South Africa (M.A.S.A.). The Second Scientific Congress of the Association of Physicians of South Africa will be held in Johannesburg on 6 - 9 July, 1960 in conjunction with the first meeting of the Society for Endocrinology, Metabolism and Diabetes of Southern Africa. The meetings will take place at the Medical School of the University of the Witwatersrand. Full details of the programme will be published as soon as they become available.

* * *

Research Forum, University of Cape Town. The next meeting of Research Forum will be held on Wednesday 20 April at 12 noon in the Bennie de Wet Lecture Theatre, A-floor, Groote Schuur Hospital, Observatory, Cape. Dr. G. S. Muller Botha will speak on 'The gastro-oesophageal closing mechanism' and will illustrate his lecture with a film. All who are interested are invited to attend this meeting.

* * *

South African Electroencephalographic Society. At a meeting of 18 persons held at the University of the Witwatersrand, Johannesburg, on 25 January 1960, the South African EEG Society was formed. The Following Council was elected—President: Prof. L. A. Hurst, Professor of Psychiatry, University of the Witwatersrand: Vice-President: Dr. A. C. Mundy-Castle, National Institute for Personnel Research, Johannesburg; Joint Hon. Secretaries: Mr. G. K. Nelson, National Institute for Personnel Research, Johannesburg, and Dr. H. E. Reef, Baragwanath Hospital, Johannesburg. There are 2 categories of membership—members and subscribers. Those interested in joining this Society are asked to communicate with the Joint Secretaries at P.O. Box 10319, Johannesburg.

NUWE PREPARATE EN TOESTELLE : NEW PREPARATIONS AND APPLIANCES

BACICORT

M.L. Laboratories announce the release of Bacicort Topical and Ophthalmic ointment, and supply the following information:

Bacicort ointment combines, in a greasy base, hydrocortisone and two antibiotics, neomycin and bacitracin. The use of neomycin and bacitracin gives Bacicort a wider antibacterial range embracing both Gram-negative and Gram-positive organisms. The addition of hydrocortisone ensures prompt relief of inflammatory conditions and the reduction of oedema, thereby producing immediate benefit and relief and, in the ophthalmic use, providing protection against functional damage.

Bacicort has been found to be of great value in the following conditions: Seborrhoeic dermatitis, adult and infantile eczema, otitis externa, contact dermatitis, pruritus vulvae and ani, and eye diseases caused by trauma, infection and allergy. Treatment is most beneficial in acute and self-limiting conditions.

Bacicort is supplied in tubes of 5 g. and 20 g. in two strengths as follows:

(1) Bacicort topical and ophthalmic ointment 1·25%—5 g. and 20 g.: hydrocortisone 1·25%, neomycin 0·5%, and bacitracin 500 u/g.

(2) Bacicort D.S. topical ointment 2·5%—5g.: hydrocortisone 2·5%, neomycin 0·5%, and bacitracin 500 u/g.

Further information can be obtained from: M.L. Laboratories, P.O. Box 2368, Johannesburg.

BOEKBESPREKINGS : BOOK REVIEWS

BACTERIOLOGY

A Textbook of Bacteriology. 8th edition, revised and enlarged. By R. W. Fairbrother, T.D., M.D., D.Sc., F.R.C.P. Pp. viii + 502. Illustrations. 25s. net. London: William Heinemann Medical Books Ltd. 1959.

The 6 years which have passed since the last edition of this book (it is now in its 8th edition) have brought about greater knowledge of bacterial metabolism, chemotherapy and virology. The present edition incorporates new developments and eliminates the obsolete. It is a clear account of the science of bacteriology necessary for the medical student and can be recommended for this purpose.

A.H.T.

MALARIOLOGY

Malariology. With special reference to Malaya. By A. A. Sandosham, L.M.S. (S'pore), Ph.D. (Lond.), F.R.E.S., F.L.S., F.Z.S., F.R.M.S. Pp. xix + 327. Illustrations. 35s. Singapore: University of Malaya Press. 1959. Sole distributors, Oxford University Press, London, New York and Toronto.

Professor Sandosham has collected in this manual in convenient form the knowledge required by malaria workers in Malaya. As such, the chapter on the natural history of anophelines and an excellent key to common Malayan anophelines is, apart from certain basic principles, of limited value to workers in other parts of the world and especially in Africa.

The rapid advances in the control and eradication of malaria is indicated by the fact that no mention is made on page 264 of Pinotti's suggestion that malaria might be controlled by the addition of an anti-malarial drug like chloroquine to all the salt consumed by the population in malarial territories—a proposal for the eradication of the malarial parasite at low cost, without expensive vector control and without fear of the development of vector resistance to the insecticides used.

The excellent chapters on basic biological information on the natural history of malaria, and on malaria surveys, control and prevention, as well as the appendices, are valuable for the instruction of students anywhere. C.J.H.B.

THE NERVOUS MECHANISM OF PAIN

Pain and Itch—Nervous Mechanisms. Ciba Foundation Study Group No. 1. Edited by G. E. W. Wolstenholme, *O.B.E.*, M.A., M.B., M.R.C.P. and Maeve O'Connor, B.A. Pp. viii + 120. Illustrations. 12s. 6d. net. London: J. & A. Churchill Ltd. 1959.

Amongst its other very useful functions the Ciba Foundation organizes study groups which meet to discuss prescribed basic scientific problems in relation to medicine. This report deals with one of the central problems of medicine—the nature of pain—and, because there is evidence suggesting a common signalling mechanism, itch is included in the survey. Pain has always had a peculiar position in sensory physiology because it may be elicited by different kinds of stimulus but it is now reasonably certain that it is subserved by special nerve fibres, the gamma and the C fibres, and not by stimulation of any sensory nerve exceeding a certain level of intensity. This report by the leading researchers in the field of sensory physiology will bring the physiologist up to date, and the clinician, who is daily presented with the problem of pain in some form or other, would do well to find time to concern himself with these new physiological investigations. S.B.

TEXT-BOOK OF SURGERY

Lehrbuch der Chirurgie. 2., Verbesserte Auflage. Herausgegeben von Prof. Dr. H. Hellner, Prof. Dr. R. Nissen und Prof. Dr. K. Vossschulte. xxxvi + 1,112 Seiten. 652 Abbildungen in 950 Einzeldarstellungen. Ganzleinen DM 84.00. Stuttgart: Georg Thieme Verlag. 1958.

In this revised and improved edition each chapter is preceded by a comprehensive historical section.

The book opens with a discussion of wound healing, including its physiology, pharmacology and sequelae. This is of special value in dealing with burns and other forms of trauma.

Throughout the book the reader is introduced to the most modern forms of treatment. Radiotherapy is adequately dealt with without monotonous detail.

The discussion of breast cancer is in line with the teaching in the major British and American clinics. The four-stage classification is used and X-ray therapy is adapted to the clinical complications or stage at the time of diagnosis.

The interesting section dealing with cardiovascular surgery and extracorporal circulation deserves special commendation.

The section on bone diseases, including benign and malignant tumours, is interesting and most instructive.

This new edition can confidently be recommended to all students of general surgery, postgraduate as well as undergraduate. D.J.H.

BRIEWERUBRIEK : CORRESPONDENCE

PHENYLKETONURIA

To the Editor: I would be very grateful if you would kindly correct a statement I made in my article 'Phenylketonuria: Report and discussion of three cases' which was published in the *Journal* of 6 February 1960.[1]

On page 114, near the bottom of the first column, I said: 'Until fairly recently no attention had been paid to phenylketonuria at this institution, . . .' This statement is the result of exhaustive enquiries and the total absence of any record of any such work ever having been done here. However, a few days ago, Dr. Lucie van Dam informed me that many years ago, when she was medical officer at this Institute, the urines of all the inmates were examined for phenylketonuria and were all found to be negative.

Walter Kluge

Alexandra Institution
Maitland, Cape
24 March 1960

1. Kluge, W. (1960): S. Afr. Med. J., 34, 113.

DIET AND CORONARY HEART DISEASE

To the Editor: I have had many enquiries about the application of recent dietary principles to the prevention of coronary heart disease.

At a symposium at the 42nd South African Medical Congress in East London I referred to Dr. Joliffe's 'prudent diet' published in the *American Journal of Clinical Nutrition*.[1] Some of your readers may have seen the book by Ancel and Margaret Keys, *Eat Well and Stay Well*.[2] Dr. Keys informs me that in the near future Hodder & Stoughton will issue a British edition adapted to British customs which may be more useful to South Africans than the American edition.

Dr. H. Gordon and I gave suggestions in an article on 'A practical dietary regime for decreasing the serum cholesterol level', published in the *Journal* in 1958,[3] and I have published an article on 'Dietary fat and coronary heart disease' in *The Practitioner*.[4]

I should mention the book *Eat Fat and Grow Slim*[5] which has started a vogue in Britain that is spreading to this country. The principle of weight reduction involved in this diet is based on a somewhat flimsy extension of short-term metabolic experiments initiated by Kekwick. The author discussed briefly the question of saturated *versus* unsaturated fat. Whatever may be the vogue in application of this method of weight reduction, there should be no question about the need to substitute a considerable quantity of unsaturated (vegetable and marine) fat for saturated (animal and artificial hydrogenated) fat to avoid hypercholesterolaemia and other lipid changes believed, on good grounds, to be responsible, in part (although only in part), for the recent increase in the prevalence of ischaemic (coronary) heart disease.

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28 March 1960

1. Jolliffe, N., Rinzler, S. H. and Archer, M. (1959): Amer. J. Clin. Nutr., 7, 451.
2. Keys, A. and Keys, M. (1959): *Eat Well and Stay Well*. New York: Doubleday.
3. Gordon, H. and Brock, J. F. (1958): S. Afr. Med. J., 32, 907.
4. Brock, J. F. (1958): Practitioner, 180, 191.
5. Mackarness, R. (1959): *Eat Fat and Grow Slim*. New York: Doubleday.

INCIDENCE OF DIABETES MELLITUS IN ONE DISTRICT OF BASUTOLAND

To the Editor: Dr. S. Sanders' letter[1] comparing the incidence of diabetes mellitus in the inhabitants of Langa Township with that which we found in the Butha Buthe district of Basutoland is particularly interesting but, we are afraid, rather misleading. In the Butha Buthe figures the incidence was obtained by comparing the number of cases of diabetes discovered in relation to the total out-patients attending Seboche Hospital. Dr. Sanders, however,

compares the number of diabetics attending the Out-patient Department of the Native Urban Hospital at the Langa Township with the total Bantu population resident in the township. It must be realized that diabetes may be symptomless and thus that not every diabetic attends the out-patient department.

In our own series none of the established diabetics attended for any complaints associated with diabetes. Actually, 3 of the cases attended for tooth extractions, and it was only as the result of routine urine testing (with blood sugar confirmation) of all out-patients attending the hospital, without reference to their complaints, that these cases were discovered.

It is therefore highly probable that the incidence of diabetes in the Langa Township is higher than the 0·22% suggested by Dr. Sanders. In fact, the work of Wilkerson and Krall[2] indicates that about half the cases may not be detected if one depends on the attendance of the diabetic at the hospital on account of his symptoms.

The conclusion is therefore inevitable that the percentage of cases at Langa is at least twice that suggested by Dr. Sanders.

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29 March 1960

1. Correspondence (1960): S. Afr. Med. J., 34, 248.
2. Wilkerson, H. L. C. and Krall, L. P. (1953): J. Amer. Med. Assoc., 152, 1322.

INCIDENCE OF DIABETES MELLITUS IN ONE DISTRICT OF BASUTOLAND

To the Editor: I was most interested to read the correspondence on this subject in your columns recently,[1,2] and should be grateful if you would allow me space to comment on it.

Though we have now 264 Bantu diabetics attending the diabetic clinic at the King Edward VIII Hospital in Durban, we have not attempted to assess the incidence of the disease from our hospital population, which, though drawn predominantly from Durban and its district, also comprises of large numbers of patients from various parts of Natal.

Of these patients, I have made a careful study of 133. To ensure that the study would be limited to a single ethnic group, I included only Bantu of the Nguni race. In the series 96% of the patients were actually pure Zulus, and the rest were Pondos and Bacas. This study was presented as a paper at the 42nd South African Medical Congress in East London in 1959.[3]

What I should like to comment on particularly, in view of Dr. Sander's remarks,[2] is the significance of the place of domicile when dealing with the incidence and aetiology of diabetes mellitus in the Bantu. I would emphasize that my series was a pure ethnic group from a circumscribed area, and it is not surprising to learn that Dr. H. C. Seftel and his colleagues in their diabetic clinic of mixed Bantu at the Baragwanath Hospital, Johannesburg, for instance, have had different findings in many respects.[4]

One thing emerged early on in the study, and that was the predominance of urban dwellers in the series, as the following table shows:

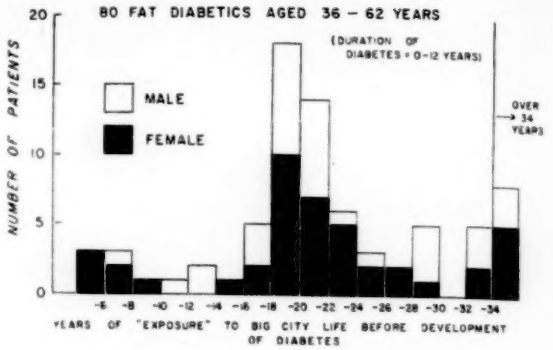
PLACE OF RESIDENCE BY DIABETIC TYPES IN 133 ZULU DIABETICS

Diabetic types	*Town dwellers**	*Country dwellers*
Senile diabetics	—	13
Middle-aged diabetics	80	8
Young insulin-dependent diabetics	19	13

* Town dwellers are defined as those who have lived in a town for over 4 years continuously before being examined.

This table shows that, not only are the majority of Zulu diabetics from the city, but that the middle-aged obese diabetic is almost exclusively from the towns. This aspect of aetiology appeared to me to be so marked, that I tried to find whether there might possibly be any constant period of 'exposure' to city life before the patients developed the disease. The following figure shows the result of this investigation in 80 fat middle-aged diabetics; it also shows how long the patients had lived in the city before developing diabetes. The duration of the disease in these cases is 0 - 12 years.

This figure shows, rather interestingly, that no less than 53% of these fat middle-aged diabetics had 'exposure' periods of between 17 and 24 years to city life before developing the disease, and that 40% had 'exposure' periods of between 19 and 22 years.



In view of the apparent effects of urbanization in the precipitation of diabetes in the Zulu, comparisons were made between the diets of the Zulus at the Lamontville Location in Durban[5] and the diet of the Nongoma peasant in Zululand. The chief differences between these 2 populations was that in the town dwellers there was an inordinate intake of sugar compared with the country peasant, whose sugar intake was actually less than 1/15th of that of the town dweller. Furthermore, the town dweller ate much more bread and fats and oils than the peasant.

In the Table it is interesting to note that the 'senile' Zulu diabetics were without exception country peasants, so much so, that in our clinic, the senile Zulu diabetic is known as the 'peasant' diabetic. In order to try to obtain some idea of how many Zulu diabetics are encountered in the Native reserves, I asked Dr. W. G. McNeil, Medical Superintendent of the large Eshowe Hospital in Zululand, for information about admissions to his hospital. He stated that the numbers of admissions for diabetes there in 1957, 1958 and 1959 were 1, 3 and 5 respectively—the annual attendance at the out-patient department being 32,000, all diabetics being admitted. He adds that the hospital drains 5 magistracies, with a total population of 400,000 Zulus, and that there is little 'bypass' of the hospital. He feels confident that the discrepancy between the incidence of diabetes in the country districts and the town can be explained by the fact that 'the rural population is as yet little influenced by European dietary habits'.

One of the more interesting findings that support the role of higher living and eating standards in the aetiology of diabetes in the Zulu, is in respect of the royal family. In spite of careful questioning, a family history of diabetes was found in less than 2% of the present series; here we differ from Seftel's clinic at the Baragwanath Hospital, where he has found a significantly higher incidence of family histories in his mixed Bantu clinic. Over the past 100 years or so, the royal family has had appreciably higher standards of living than their subjects. Since the passing of the great militant kings and beginning with the enormously fat Mpande, the royal family have lived in comparative ease, and their obesity has been legendary. In this family there is a very marked history of diabetes, both in the direct and in the cadet lines. Furthermore, as 2 of the wives of members of the royal family are diabetics in their own right, the accession of a diabetic would appear assured!

From my observations on the aetiology of diabetes mellitus in the Zulu, I feel confident that the higher standards of living and eating (epitomized by the urban dweller) are powerful aetiological factors in the genesis of the disease in the Zulu race. I regret greatly that, as yet, I am unable to give any indication of the incidence of the disease in the nation as a whole.

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31 March 1960

1. Correspondence (1960): S. Afr. Med. J., 34, 188.
2. *Idem* (1960): *Ibid.*, 34, 248.
3. Campbell, G. D. (1959): Paper on *The Zulu Diabetic* read at the 42nd South African Medical Congress (M.A.S.A.), East London, September - October 1959.
4. Seftel, H. C. (1960): Personal Communication.
5. Gampel, B. (1960): Personal Communication.